New Fundamental and Clinical Perspectives on Abdominal Wall Hernia Research

Yağmur Yurtkap

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Colophon

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New Fundamental and Clinical Perspectives on Abdominal Wall Hernia Research

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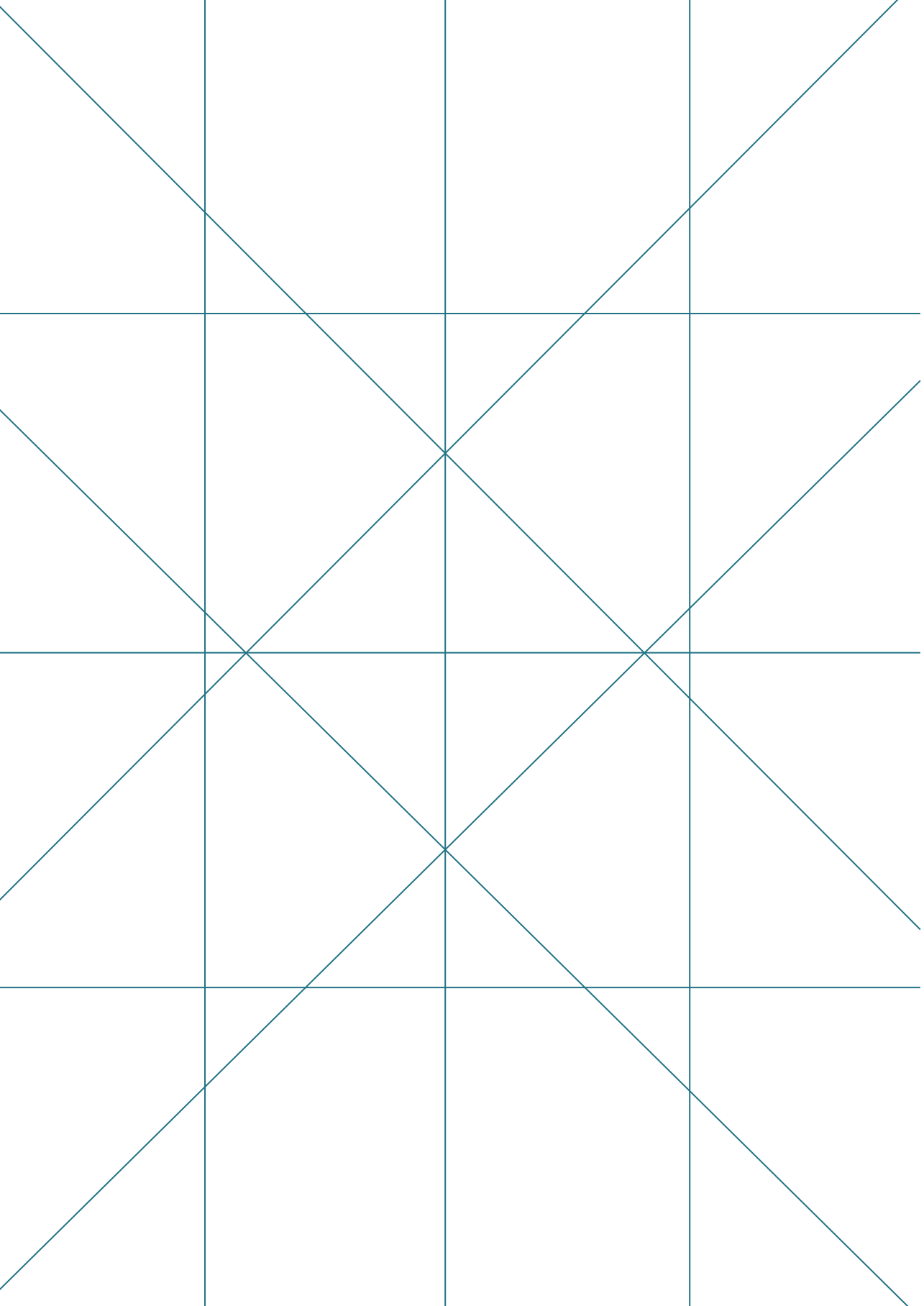

Chapter 1

General introduction

Anatomy of the abdominal wall

The embryo is an elongated disk which evolves into a cylindrical form after three to four weeks of pregnancy [1]. The endoderm forms the neural tube. In contrasting direction with the endoderm, the ectoderm and mesoderm form the frontal body wall and the gut tube. Finally, the mesoderm turns into the muscles and the fascia of the abdominal wall at ten weeks of gestation. In a fully grown human, the abdominal wall includes the skin, subcutaneous fat, superficial fascia, fat, muscles, transversalis fascia, preperitoneal fat, and the peritoneum. The abdominal wall, consisting of a combination of several muscle layers and connective tissue, surrounds the abdominal cavity with its organs. The two vertical rectus abdominis muscles come together in the midline to form the *linea alba.* The *linea alba,* translated as the white line, extends from the xiphoid process to pubic symphysis and consists of the combined aponeuroses of the lateral muscles, *i.e.* the external and internal oblique muscles and the transversus abdominis muscle. The *linea alba* is scarcely vascularized and consists of three layers of collagen fibers (hence the name 'white line') with three fiber orientations corresponding to the three lateral muscles. The rectus muscles are provided with blood by the superior and inferior epigastric arteries, deriving from the internal thoracic and external iliac arteries. Innervation is supplied by the intercostal nerves. Extensive knowledge of the morphology of the abdominal wall is important for any surgeon, since laparotomy will be performed mostly through the *linea alba.* The function of the abdominal wall is to protect the organs in the abdomen, to enable movement of the torso and to facilitate breathing. The abdominal wall muscles are mainly activated during expiration [2]. During active breathing, for example during exercise, all these muscles are involved. The muscles of the abdominal wall contract and move in the dorsal direction, leading the diaphragm to move cranially, stretching the inferior ribs caudally for deflation of the lungs.

Incisional hernia

An abdominal wall hernia is an aponeurotic defect with intermittent or continuous protrusion or bulging of fat or abdominal organs through the abdominal wall. Research in this thesis focuses on defects through the *linea alba.* Abdominal wall hernias may be present as a congenital, acquired or iatrogenic condition. An iatrogenic hernia, generally known as an incisional

hernia or hernia cicatricalis, is a common complication after abdominal surgery. The definition of an incisional hernia according to the European Hernia Society (EHS) is: "Any abdominal wall gap with or without a bulge in the area of a postoperative scar perceptible or palpable by clinical examination or imaging." [3]. Incisional hernia has a variability in incidence of two to 20 per cent, increasing up to over 30 per cent in high risk patients [4-8]. Patients with a higher risk of developing an incisional hernia are mostly defined as patients with a body mass index of higher than 27 kilograms per square meter or with an aneurysm of the abdominal aorta [5, 9]. Patients with an incisional hernia may be asymptomatic or suffer from pain, discomfort and a negatively impacted quality of life [10]. Emergency surgery for hernia repair may be necessary in case of incarceration or bowel strangulation, which is associated with morbidity and mortality [11]. Surgical outcomes after incisional hernia repair have improved after the introduction of mesh repair; nevertheless, recurrence rates remain high. The recurrence rate after primary incisional hernia repair is up to 64% and 32% after mesh repair [12]. Additionally, the occurrence of an incisional hernia can, apart from affecting patient-related health outcomes, also result in a financial burden for the healthcare system [13].

Risk factors and treatment

Risk factors for developing an incisional hernia are based on patient characteristics, technical determinants and postoperative factors. Patient characteristics, such as obesity, diabetes mellitus and connective tissue disorders, can hinder regular wound healing and increase the risk of the development of incisional hernia. Patients with obesity (body mass index $\geq$ 30 kilograms per square meter) and/or, an aneurysm of the abdominal aorta are broadly studied patient populations with a higher risk of incisional hernia formation [14, 15]. Technical and postoperative factors, such as too high or too low tension on sutures, or surgical site infection, may result in hernia formation. Surgical site infections are known to double the chance of incisional hernia development [16]. One may conclude that these factors, which are only several examples out of a large number of factors, contribute to impaired wound healing, raised intra-abdominal pressure and strain on the abdominal wall. To

date, the standard treatment for abdominal wall hernia (primary or incisional) is tension-free fascial closure with mesh augmentation [17]. Mesh placement in several anatomically defined planes can be considered, depending on the type and location of the hernia, and the surgeon's experience [18]. This, in combination with the many types of mesh that are on the market and the lack of evidence, makes it difficult to determine which mesh is supposed to be used in which situation. Currently, a personalized approach is only on the horizon.

Complex hernias

A plethora of mesh types is available and different meshes are to be used in different situations. Finding the optimal type of mesh for every one of these situations remains an ongoing process. Giant and potentially contaminated or infected hernias are considered complex hernias [19-22]. In case a patient is classified in a potentially contaminated or infected category, using a regular non-absorbable synthetic mesh is controversial, given the higher risk of wound healing problems and possible need for mesh removal [16]. On the contrary, evidence shows that the controversy of using a synthetic mesh in potentially contaminated or infected areas might be unfounded [23]. Another option is the use of a biologic mesh for these specific patients [24]. However, high-level evidence, especially with regard to the intensity and quality of remodeling, is lacking and the much higher cost compared with synthetic meshes is, in this respect, a disadvantage [25]. Another category of complex hernias is represented by large or giant abdominal wall hernias with a diameter greater than ten centimeters with or without loss of domain [3, 19]. In case of loss of domain, the abdominal cavity is unable to house the abdominal contents within its fascial borders [26]. As a result of this, reduction of the abdominal organs into the abdominal cavity after hernia correction, can result in pulmonary dysfunction. In large abdominal wall hernias, additional medialization of the rectus muscles may be necessary to achieve fascial closure. The Rives-Stoppa and the anterior and posterior component separation techniques are available for large or giant abdominal wall hernias [27]. In some cases, these component separation techniques are not sufficient to achieve fascial closure. Fortunately, preoperative methods, such as the use of botulinum toxin A and progressive pneumoperitoneum, are also available as an addition to component separation techniques in order to be able to close the abdominal fascia tension-free.

Prevention and biomechanics

Primary prevention of the occurrence of an incisional hernia is clearly an important topic at both patient- and socioeconomic levels. As mentioned earlier, in addition to patient characteristics, surgical techniques and suture materials for the closure of the fascia of the abdominal wall are relevant determinants for prevention and treatment. A continuous positive pressure of zero to twenty mm Hg is maintained inside the abdominal cavity, which may increase up to 320 mm Hg with the Valsalva maneuver [28-30]. Postoperatively, the intra-abdominal pressure may increase (*i.e.* due to postoperative ileus), resulting in an up to 30 per cent increase in abdominal circumference [31]. In order to minimize the increasing tension in and between the sutures due to the postoperative status, suture material length of at least four times the wound length (suture length to wound length ratio of four to one or more) is recommended [31]. In a clinical randomized trial including 560 patients, suture length to wound length ratio of four or more or the small bites technique, compared with the large bites technique, for fascial closure resulted in a decrease in incisional hernias (21% *versus* 13%) after a follow-up of one year [32]. The inclusion of less tissue into the bites could result in a better distribution of strains and forces and less tissue necrosis by preventing ischemia. In this thesis, the underlying biomechanical mechanisms underlying the small bites technique will be investigated. Additionally, the creation of a suture tension sensor in order to measure the tension while or after closing the *linea alba* was attempted. In our opinion, an incidence of 13% of incisional hernias using small bites for closure is still unacceptable. The search for finding even better closure patterns and suture materials is ongoing in order to decrease this incidence even further.

The aim of this thesis

The aim of this thesis was to contribute to the ongoing search for improving closure techniques of the *linea alba* and to prevent the occurrence of incisional hernia. The understanding of the fundamental mechanisms underlying closure methods and incisional hernia formation forms the basis of this thesis. The second aim was to investigate the treatment of complex or giant hernias in experimental set-ups. Lastly, prevention and treatment of simple and complex hernias were investigated.

Outline of this thesis

In **chapter 1** a general introduction on abdominal wall hernias is given.

In ***part 1*** of this thesis, a search for fundamental knowledge in biomechanics for abdominal wall closure is performed.

In **chapter 2** strain patterns after several midline closure techniques are investigated in *post mortem* human specimens.

In **chapter 3** suture tension in a new suture material is measured with the use of a suture tension sensor in porcine abdominal walls.

In ***part 2*** of this thesis, fundamental experiments are performed for better understanding closure techniques and improving the treatment of complex hernias.

In **chapter 4** medialization of the rectus muscles is measured after utilizing the Rives-Stoppa technique, anterior component separation and posterior component separation techniques in *post mortem* human specimens. In this study, a comparison in medialization is made between different hernia repair techniques available for large hernias.

In **chapter 5** zinc-impregnated meshes are investigated in a rat model with peritonitis in **chapter 5**. Meshes with zinc impregnation may be a solution for hernia repair in (potentially) contaminated patients.

In ***part 3*** of this thesis, clinical research in hernia prevention and treatment is performed.

Chapter 6 is a book chapter, in which an overview of the prevention of incisional hernia is given. Emergency surgery has poor surgical outcomes with high morbidity and even mortality.

In **chapter 7** risk factors for incarceration (and possibly requiring emergency surgery) in primary abdominal wall and incisional hernias are investigated in a prospective study.

In **chapter 8** a cohort of 23 patients with giant hernias with loss of domain and the use of botulinum toxin A and preoperative progressive pneumoperitoneum in addition to component separation techniques is described.

In **chapter 9** functional outcomes in symptomatic and asymptomatic patients with incisional hernia repair are studied.

In **chapter 10** and **chapter 11** the findings of this thesis are summarized and discussed. Additionally, recommendations for the future in fundamental research and for clinical practice are provided.

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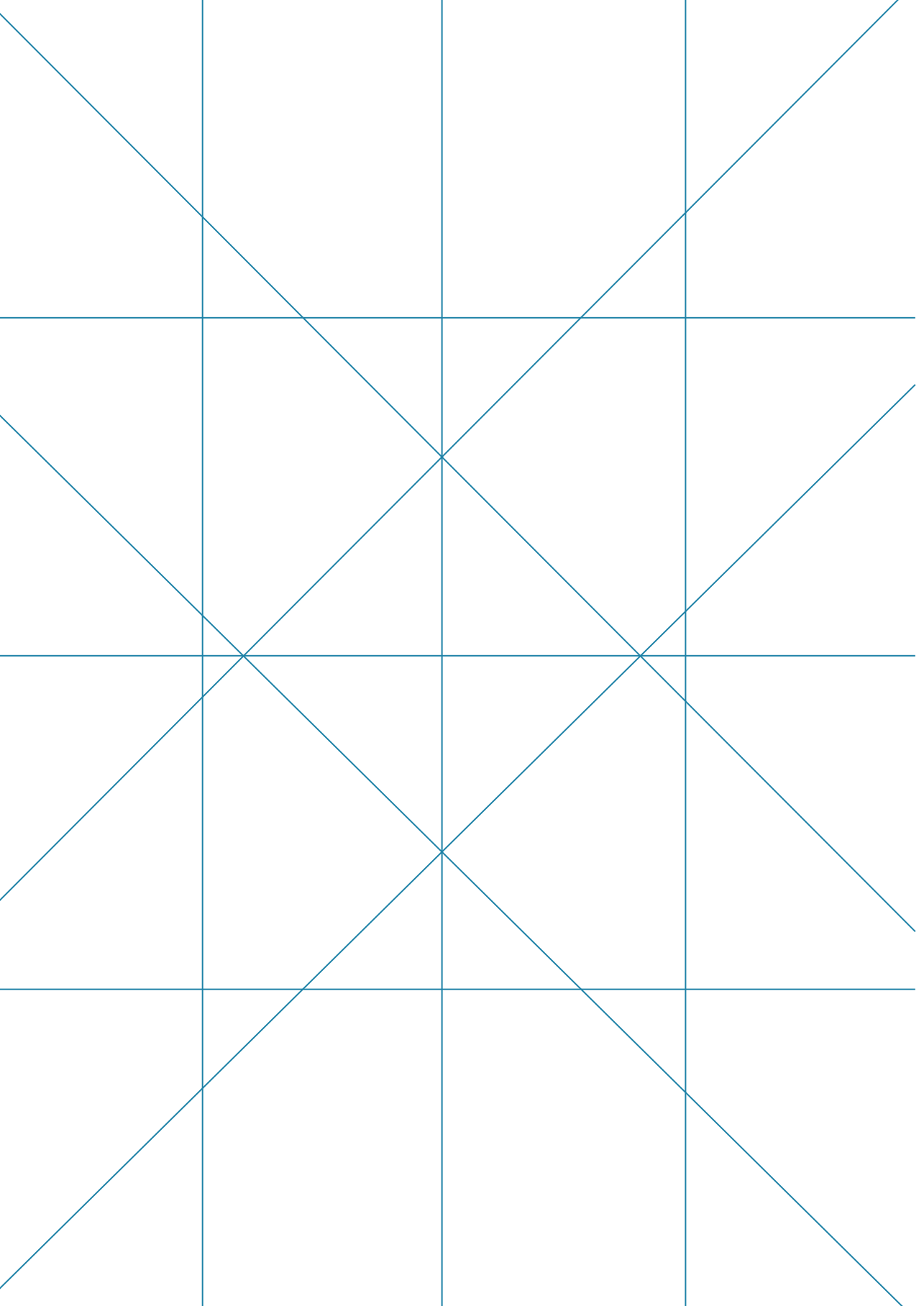

Part I

Fundamental Knowledge in Biomechanics for Abdominal Wall Hernia Closure

Chapter 2

Differences in biomechanics of abdominal wall closure with and without mesh reinforcement: a study in post mortem human specimens

Y. Yurtkap, A. Le Ruyet, F.P.J. den Hartog, A. Vegleur, F. Turquier, J.F. Lange, G.J. Kleinrensink

Y. Yurtkap and A. Le Ruyet contributed equally to this work.

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Abstract

Introduction

Small bites for the closure of the abdominal wall after midline laparotomy result in significantly less incisional hernias in comparison with large bites. However, fundamental knowledge of underlying biomechanical phenomena remains sparse. The objective of this study was to develop a digital image correlation-based method to compare different suturing techniques in terms of strain pattern after closure of a midline laparotomy in a passive model just after the time of surgery.

Methods

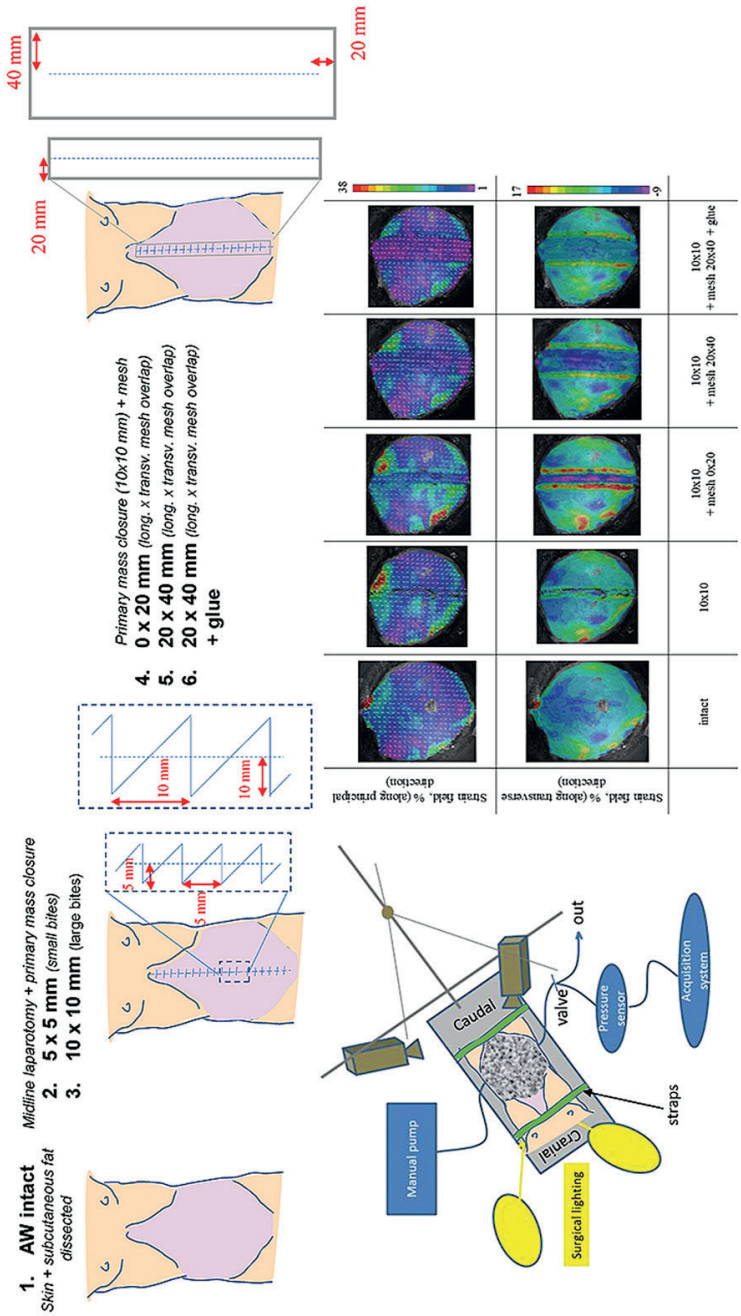
A digital image correlation (DIC)-based method was used for the comparison of strain fields on the external surface of the myofascial abdominal wall (skin and subcutaneous fat removed) among six configurations, including an intact *linea alba* in five *post mortem* human specimens. The second configuration comprised primary mass closure with small bites (five mm between two consecutive stitches and five mm distance from the incision, 5x5 mm). The third configuration was primary mass closure with large bites (ten mm by ten mm, 10x10 mm). The fourth, fifth and sixth configuration comprised primary mass closure with large bites and the placement of a mesh in onlay position with two different overlaps and the use of glue to simulate the integration of the mesh within the soft tissue.

Results

No visible difference was observed between 5x5 and 10x10 mm closure configurations. However, the use of mesh as suture line reinforcement highlighted a stiffer behavior of the midline area for similar intra-abdominal pressure, which was amplified when a larger mesh overlap was used. However, the whole abdominal wall showed quite similar shapes for the various configurations, except for the configuration with mesh reinforcement and the use of glue.

Conclusion

Mesh reinforcement incited lower opening tension profiles in the midline area of the abdominal wall. following closure of the *linea alba* in median laparotomy. The next step should be to investigate the impact of mesh location (*e.g.* retromuscular) and different time points after surgery.



Graphical abstract

Introduction

Incisional hernia remains one of the most frequently occurring complications of abdominal surgery, with an estimated occurrence of 5–20% [1, 2]. Incisional hernia can lead to increased morbidity, mortality and diminished quality of life [3]. An estimated number of 300.000 incisional hernia repairs are performed each year in the USA alone [4]. Therefore, the prevention of incisional hernia after laparotomy is of high importance.

In a recent randomized controlled trial, the conventional large bites (*i.e.* 10 mm between two stitches and 10 mm from the wound edge) were compared with the small bite technique (*i.e.* 5 mm by 5 mm). This study showed that small bites were more efficient for the prevention of an incisional hernia after midline incisions, after a follow-up of one year [5]. However, the incidence of incisional hernia still remains high with 13% at one-year follow-up [5]. As such, the search for the optimal midline incision closure technique is justified. Additionally, in high-risk groups, such as patients with obesity or an aneurysm of the abdominal aorta, the incidence of an incisional hernia after midline laparotomy may increase up to 69% [6]. The use of a prophylactic mesh for the closure of a midline incision in this high-risk population has been suggested for the reduction of the incidence of an incisional hernia [7, 8].

Closure techniques for abdominal wall midline incisions have been investigated by many authors. Closure continuity, size of suture stitches and suture distance from the incision were shown to play significant roles in successful abdominal wall closure preventing incisional hernia [9-11]. Running sutures with shorter stitch distance are usually associated with lower rate of both wound infection and incisional hernia [12, 13]. Running sutures with a suture length to wound length ratio higher or equal to 4:1 and low suture tension promote collagen synthesis in the incisional region [14]. Small stitches with small suture distances resist higher tensile forces than large stitches with large suture distances and, thus, may better prevent the burst abdomen or incisional hernia [15]. In a recent study including 48 *ex vivo* porcine abdominal walls, small bite separation (5 mm) and large bite width (16 mm) were shown to be optimal for abdominal wall using a criterion based on pullout strength [16]. One limitation of most of these studies is the use of *ex situ* samples which

decreases the biofidelity of the used boundary conditions. There is a need to establish connections between the closure configuration, the biomechanical response of the abdominal wall *in situ* and the remodeling process at different time points after the closure. This fundamental, biomechanical knowledge may form the basis of discovering the optimal closure technique. Podwojewski *et al.* demonstrated the feasibility of this measurement technique to differentiate the mechanical response of the abdominal wall when several configurations were tested (*i.e.* intact, incised along the midline and repaired) [17]. The objective of this present study was to compare the mechanical response of the abdominal wall *in situ* to different suturing techniques after midline laparotomy with an intact *linea alba* in a *post mortem* human passive model using a digital image correlation (DIC)-based method.

Materials and methods

All experiments were performed on five fresh frozen *post mortem* human specimens (PMHS). Consent to donation for scientific or educational programs had, according to Dutch law, been given prior to passing away. No data on medical history were available about the included PMHS due to European procedures. All experiments were performed at the Anatomical Department of the Erasmus University Medical Center in Rotterdam. PMHS with noticeable or palpable scars or herniations in the abdominal wall were excluded. Prior to the surgical procedure, anthropometric data of the PMHS were measured (*i.e.* waist circumference, distance between iliac crests, distance from xiphoid process to the pubic bone, chest, waist and buttock depth).

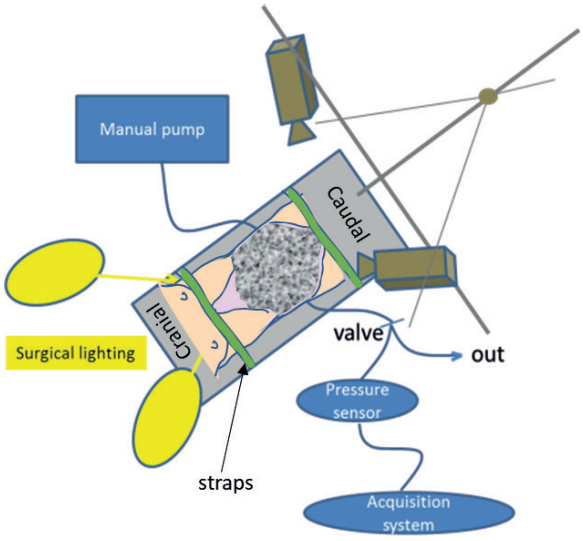
PMHS preparation

Before the preparation, the PMHS was thawed at room temperature for 48 hours. The skin was incised along the midline from the xyphoid process to the pubic bone. The subcutaneous tissue was dissected carefully without damaging the fascia and the *linea alba* was identified. Subsequently, two drains were inserted into the peritoneal cavity in the right and left flank, between the most caudally palpable rib and the anterior superior iliac spine. These drains were fixed in the abdomen in an air-tight fashion using sutures (Mersilene, 2-0, Ethicon, Belgium) and the tobacco-pouch suturing technique. Before each test, white painting, used for cosmetics, was manually applied on

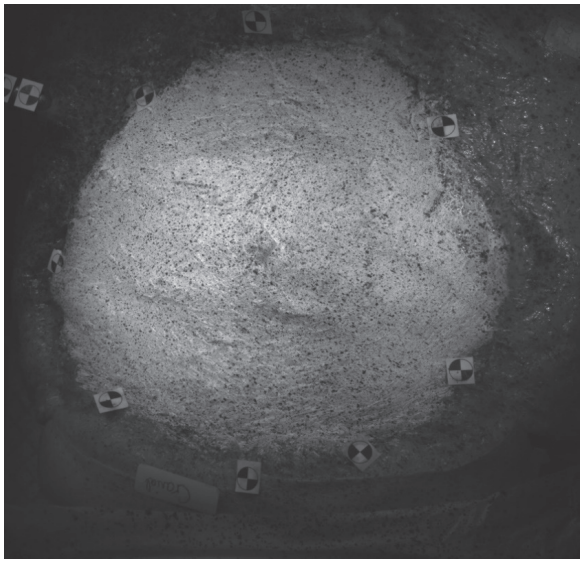
the anterior rectus sheath and on the external surface of the external oblique muscle. Then, a random black pattern was spray-painted to create a stochastic pattern of dots.

Test setup

An overview of the test setup is shown in Figure 1. The PMHS was placed in the supine position on a rigid operating table. Ratchet straps were applied tightly around the ribcage and the pelvis to minimize motion of the bony structures surrounding the abdominal wall during the tests. Two charge-coupled device (CCD) cameras (CC-044, CMOSIS CMV4000) mounted with two 28-mm-length zoom lenses (Schneider Kreuznach) were used to capture the response of the abdominal wall during the tests. The resolution of the cameras was equal to 2048x2048 pixels, which allocated approximately five to six pixels per millimeter in the region of interest. Two surgical lights were used to ensure good contrast of the recorded images. The two CCD video cameras were placed above the PMHS to provide frontal views of the abdomen during the tests. The frame rate was set to ten images per second and the pair of cameras was calibrated in three dimensions (3D). The cameras were positioned to cover the entire abdominal region. Target markers on printed paper were placed on the operating table around the PMHS to define the origin of the antero-posterior direction. The reference frame used for this study was defined by the position of the cameras: the X-axis (referenced further as transverse direction) was defined as parallel to the segment going through each camera optical center. The Y-axis (referenced further as longitudinal axis) was defined as perpendicular to the X-axis within the mean plane of the camera sensors. The Z-axis (referenced further as the antero-posterior direction) was defined as perpendicular to the X- and Y-axis previously defined. One of the drains was inserted into the peritoneal cavity, connected to a pressure transducer (0.35 bar, EPX-N02–0.35B, Measurement Specialties™) which in turn was connected to a data acquisition system (Sirius ®, DEWESoft ®). The other drain was connected to a manual pump in order to insufflate the abdominal cavity. The pressure was recorded during the test and could be visualized in real time by the operator. The inflation was stopped as soon as 40 mm of mercury (mmHg) was reached. Simultaneously, images of the response of the abdominal wall were recorded. At the end of each test, the abdominal cavity was deflated.



(a)



(b)

Figure 1. Schematic view of the experimental setup (a) and picture (b) recorded by one camera showing the speckle pattern and white painting applied on the anterior myofascial surface (PMHS #6, intact configuration). The marker visible in the right bottom corner was used to define the origin of the antero-posterior direction.

Test matrix

Twenty-five consecutive pressure cycles were applied to one, intact PHMS (#1) as a control, in order to assess the response of the intact abdominal wall in terms of strain fields. Six different configurations were performed on the remaining four PMHS. The pressure loading cycle was repeated three times.

1. Intact abdominal wall

   A midline laparotomy was performed from the xiphoid process to the pubic bone and five configurations were performed as follows:

2. Primary mass closure with USP 2-0 PDS Pl us II (Ethicon, Sommerville, NJ, USA) with a 31 mm needle with 5 mm between two consecutive stitches and 5 mm distance from the incision was performed. Before closing, dots showing the needle crossing points were painted on the anterior fascia. This configuration will be referenced further as 5x5.

3. Firstly, stitches from the second configuration (5x5) were removed. Primary mass closure with USP 2-0 PDS Plus II (Ethicon, Sommerville, NJ, USA) with a 31 mm needle with 10 mm between two consecutive stitches and 10 mm distance from the incision was performed. Before closing, dots showing the needle crossing points were painted on the anterior fascia. This configuration will be referenced further as 10x10.

4. Primary mass closure with USP 2-0 PDS Plus II (Ethicon, Sommerville, NJ, USA) with a 31 mm needle with 10 mm between 2 consecutive stitches and 10 mm distance from the incision was performed (configuration 3). A mesh with polypropylene yarns in onlay position with 0 mm overlap in cranial and caudal direction and 20 mm overlap in the lateral direction was placed. The mesh was fixated using interrupted stitches (USP 2-0 PDS Plus II (Ethicon, Sommerville, NJ, USA). This configuration will be referenced further as mesh 0x20.

5. Primary mass closure with USP 2-0 PDS Plus II (Ethicon, Sommerville, NJ, USA) with a 31 mm needle with 10 mm between two consecutive stitches and 10 mm distance from the incision was performed (configuration 3). The mesh from the fourth configuration (mesh 0x20)

was removed. A mesh with polypropylene yarns in onlay position with 20 mm overlap in cranial and caudal direction and 40 mm overlap in the lateral direction was placed. The mesh was fixated using interrupted stitches (USP 2-0 PDS Plus II (Ethicon, Sommerville, NJ, USA). This configuration will be referenced further as mesh 20x40.

6. Primary mass closure with USP 2-0 PDS Plus II (Ethicon, Sommerville, NJ, USA) with a 31 mm needle with 10 mm between two consecutive stitches and 10 mm distance from the incision was performed (configuration 3). A mesh with polypropylene yarns in onlay position with 20 mm overlap in cranial and caudal direction and 40 mm overlap in the lateral direction was placed. The mesh was fixated using interrupted stitches (USP 2-0 PDS Plus II (Ethicon, Sommerville, NJ, USA) and cyanoacrylate glue (Loctite 495, Henkel Corporation, United States) to simulate the integration of the mesh in the surrounding soft tissues. This configuration will be referenced further as mesh 20x40+glue

Due to the protocol complexity, each PMHS was tested over two consecutive days. The first day was dedicated to the preparation of the specimen and the next day to testing. The PMHS was stored on a cooling plate during the night and preserved for the next day. Ultrasound gel and gauzes soaked in sodium chloride were applied on the external surface of the abdominal wall to maintain the soft tissue hydration.

Data analysis

The images captured by the cameras were processed using commercial digital image correlation (DIC) software (Vic-3D™, Correlated Solutions) to assess three dimensional (3D) fields such as displacement, strain or curvature over the external surface of the abdominal wall. The parameters used are listed in Table 1. The regions of the images exhibiting artifacts (mostly along the midline) were removed by thresholding the raw data derived from DIC analysis. As such, the consistency threshold, the confidence margin, and the matchability threshold were set to 0.1 pixels. The reference image (representing the initial

state) was defined when the intra-abdominal pressure measured was equal to two mmHg. This was done to mitigate the occurrence of artifacts during the DIC analysis due to soft tissue unfolding at the beginning of the inflation. The displacement, along the cranio-caudal and the antero-posterior directions of points around the xiphoid process and the pubic symphysis were extracted (Figure 2). The following outputs were defined as comparison criteria between closure modalities: 1) the profile of the abdominal wall in both longitudinal and transverse directions; 2) the point located on the midline 3 cm cranially to the umbilicus throughout the inflation and estimated as a function of the pressure based on the position fields; 3) strains averaged over one four-cm-width rectangle, from the xiphoid process to the umbilicus, centered on the midline as a function of the pressure (Figure 2).

Subset size	35 x 35 pixels
Step size	7 pixels
Strain filter size	15 pixels

Table 1. Parameters used for image analysis

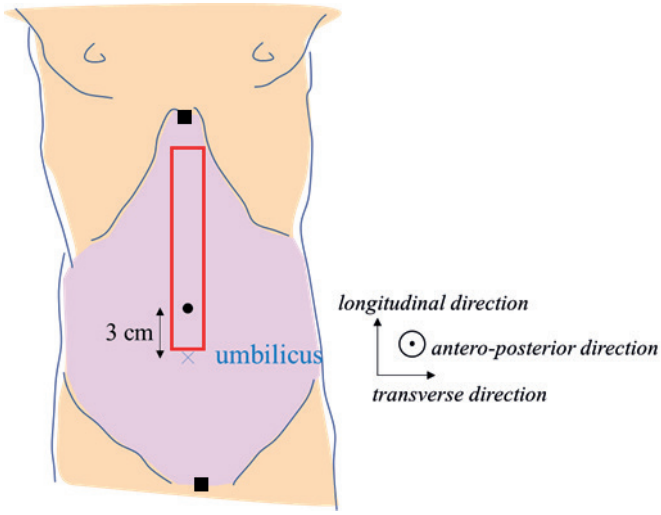


Figure 2. Localization of strain measurements (red rectangle) and position measurement (point located on the midline 3 cm cranially to the umbilicus). Black squares show the location of the points picked to assess the displacement of the xiphoid process and the pubic symphysis.

Results

Finally, six PMHS were included in this study, with three male specimens and three female specimens. One PMHS (#3) was excluded from this study due to extreme atrophy of the abdominal muscles. All dimensions of the five included PMHS were listed in Table 2. After dissection and removing of the skin and the subcutaneous fat, one PMHS (#1, control) exhibited a ventral hernia with a diameter of 5 mm, located para-umbilically. The protocol described before was successfully applied to the remaining four PMHS (PMHS #2, PMHS #4, PMHS #5 and PMHS #6). For PMHS #2, it was attempted to study the configuration mesh 0x20 + glue just after the configuration mesh 0x20 was tested. However, the application of glue on the mesh and the soft tissue made the study of the rest of the configurations difficult. The removal of the mesh glued to the surrounding soft tissue altered the tissue strongly. Therefore, it was decided to study the effect of the glue as a final test only for the other PMHS (configuration mesh 20x40 + glue). For all PMHS, minor air leakage was observed at the insertion area of the flexible drains into the abdominal cavity. However, this was compensated by adjusting the manual pumping and the pressure target (40 mmHg) was reached for each test.

PMHS	**1**	**2**	**4**	**5**	**6**	**Median, range (mm)**
Gender	M	F	M	M	F	Not applicable
Waist circumference (mm)	850	840	880	912	1020	880 (840 - 1020)
Distance iliac crests (mm)	270	230	280	295	320	280 (230 - 320)
Xiphoid to pubis (mm)	280	290	340	310	390	310 (280 - 390)
Chest depth (mm)	220	210	230	215	240	220 (210 - 240)
Waist depth (mm)	150	160	220	175	220	175 (150 - 220)
Buttock depth (mm)	160	200	195	190	185	190 (160 - 200)

PMHS **Abdominal wall thickness**	**1**	**2**	**4**	**5**	**6**	**Median, range (mm)**
Supra-umbilical (mm)	4	4	4	3	7	4 (3 - 7)
Umbilical (mm)	6	5	5	4	7	5 (4 - 7)
Infra-umbilical (mm)	8	5	6	5	5	5 (5 - 8)
Lateral (mm)	3	4	8	5	5	5 (3 - 8)

Table 2. Dimensions of five includes PMHS

PMHS #1: control

Twenty-five pressure cycles were successfully submitted to PMHS #1 over one day. The position along the antero-posterior direction and strain fields (Green-Lagrange strain) of the external surface of the abdominal wall for the tests one and 25 are shown in Figure 3. Qualitatively, position fields and profile views looked similar for these two tests. Minor differences were distinguished and were located towards the edges of the region of interest and could be due to numerical artifacts as a result of the DIC-based method. Strain fields showed more differences between test one and 25. Although the strain patterns (*e.g.* principal direction oriented in the cranio-caudal direction) were similar for these two tests, differences were distinguished regarding the strain amplitude, in particular for the cranial part of the abdominal wall. It was observed that strain amplitude decreased, highlighting a stiffening of the external surface of the soft tissue as pressure cycles were applied. However, it should be noted that the random speckle pattern was the same for all tests; it was not reapplied. The paint drying process could explain the stiffening process observed.

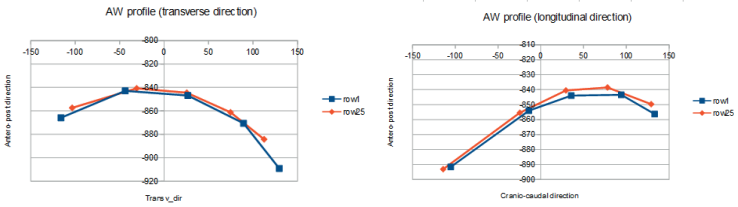
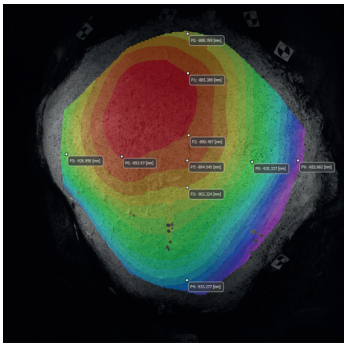
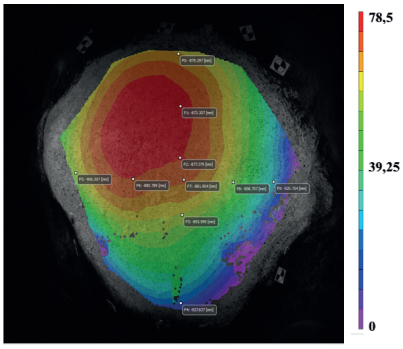
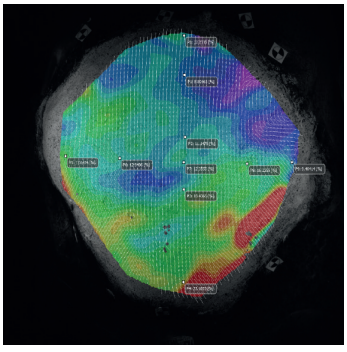
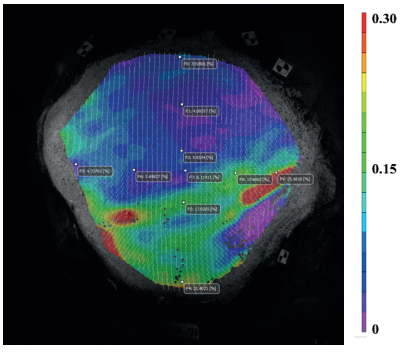
	Row 1 (40 mmHg)	Row 25 (40 mmHg)
Profile view along the longi-tudinal and transverse directions		
Position fields (mm) along the antero-posterior direction		
Strain fields along the first principal direction		

Figure 3. Profile view, position and strain (Green-Lagrange) fields of the external surface of the abdominal wall for the tests one and 25 (PMHS #1, control)

PMHS #2 #4 #5 #6

Each PMHS was successfully subjected to three pressure cycles for each of the six configurations (a total of 18 pressure cycles) and the response of the abdominal wall was evaluated for each closure configuration. The displacement of the xiphoid process and the pubic symphysis along the cranio-caudal and the antero-posterior directions are plotted as a function of the pressure for the intact configuration only in Figure 4. The displacement of the pubic symphysis was very limited in both antero-posterior and cranio-caudal directions (<3 mm) whereas the displacement of the xiphoid process was higher in both directions. The displacement of the xiphoid process was up to 25% of the initial chest depth and up to 30 mm was measured along the antero-posterior and cranio-caudal directions, respectively. The displacement of these bony structures did not vary linearly as a function of the pressure: a relatively rapid increase of the cranial and ventral motion occurred from 0 to 15 mmHg, which slowed down from 15 mmHg to 35 mmHg without stopping movement over this range.

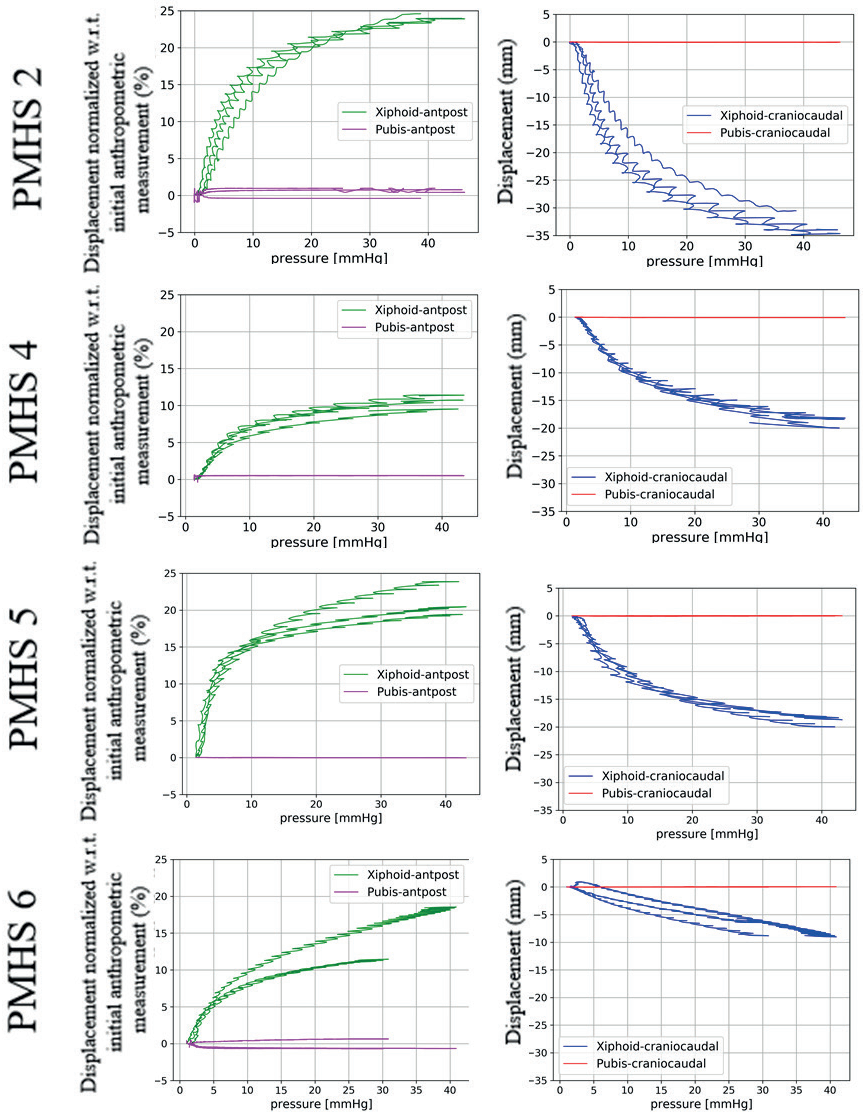
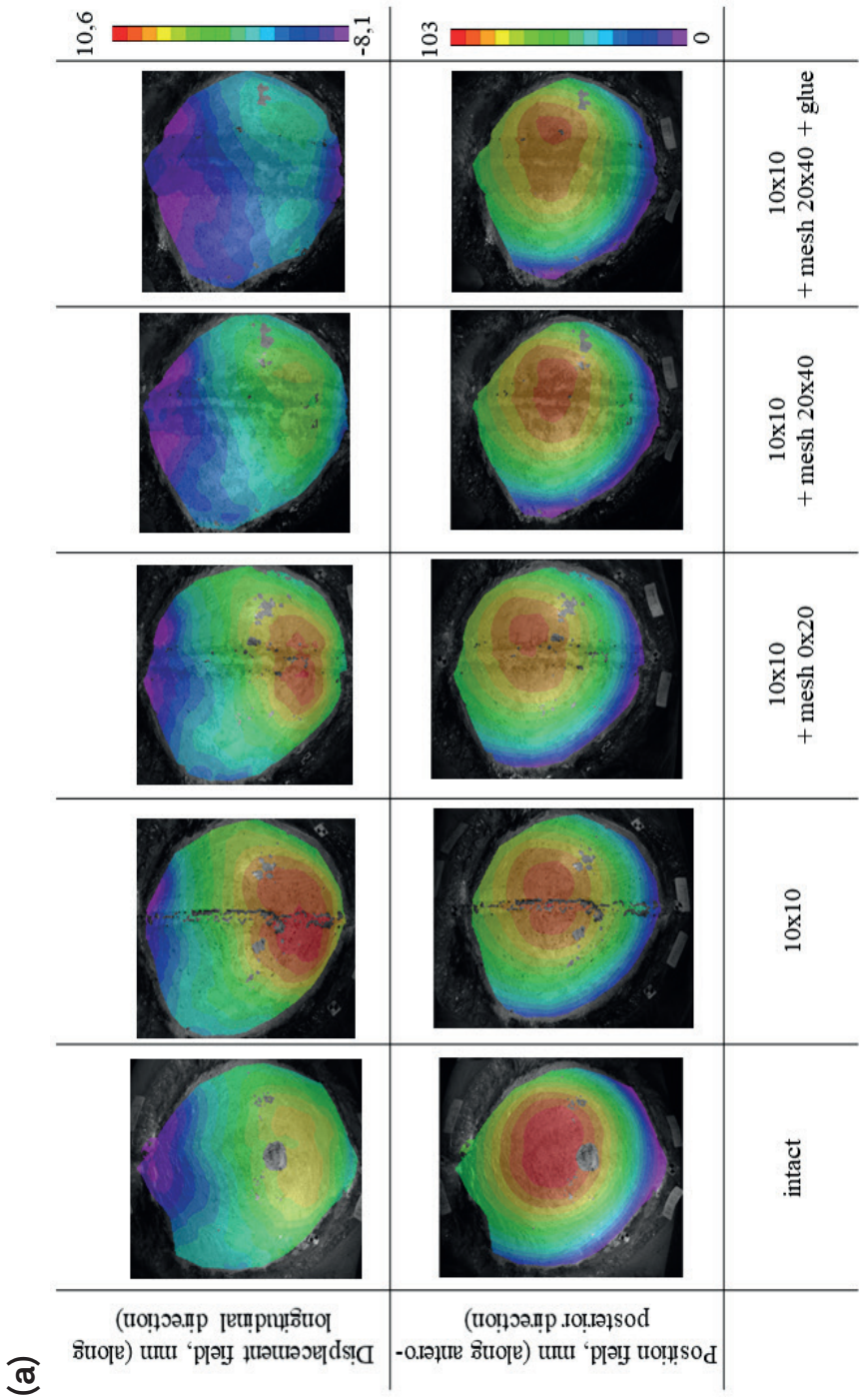


Figure 4. Displacement of the xiphoid process and the pubic symphysis for each PMHS along the cranio-caudal and antero-posterior directions. The displacement values along the antero-posterior direction were normalized with respect to (w.r.t.) the chest depth and the waist depth measured on the PMHS. Y-axis: positive and negative displacement are ventral and dorsal respectively (antero-posterior direction) and caudal and cranial respectively (cranio-caudal direction).

Position and displacement fields at maximum pressure inflation in the antero-posterior direction and the cranio-caudal direction, respectively, for PMHS #6 are shown in Figure 5a. Results are shown for the following closure configurations: intact, 10x10 and the use of a mesh with an overlap equal to 0x20 mm, 20x40 mm and 20x40 mm combined with the use of glue. Overall, the shape of the position fields along the antero-posterior direction looked similar for the three configurations showing a dome-like shape of the abdominal wall. Regarding the amplitude, differences were more marked with higher amplitude for the intact configuration in comparison with other configurations (10x10, mesh 0x20, mesh 20x40 and mesh 20x40 + glue). The displacement fields along the cranio-caudal axis exhibit cranial motion of the most cranial part of the abdominal wall for each configuration (about 8 mm). Caudal motion can be observed around the region just caudally to the umbilicus. The configuration 10x10 exhibits the highest motion amplitude along this direction (about 11 mm) whereas this was more limited for the configuration mesh 20x40 + glue. For the same configurations (*i.e.* intact, 10x10, 10x10 + mesh 0x20, 10x10 + mesh 20x40 and combined with the use of glue), strain fields (Green-Lagrange) in the principal and the transverse directions are shown in Figure 5b. Overall, strain fields differed largely in terms of shape and amplitude for these five configurations. These five configurations led to principal strains mostly oriented in the longitudinal direction. The intact configuration led to higher amplitude strains along the transverse direction over the lateral parts (external oblique) in comparison with the anterior rectus sheath. Orientations in the transverse direction were seen on the lateral parts of the region of interest, corresponding to the external surface of the external oblique muscle. Different strain patterns were observed among the five configurations especially around the midline. The intact configuration exhibited homogeneity in this region whereas for the 10x10 configuration, high-amplitude patterns were visible. Concerning the configuration using reinforcement with a mesh, high-amplitude patterns were visible along the lateral edges of the mesh. However, it should be noted that these high-amplitude patterns may also result from sliding between the mesh and the abdominal wall, which are considered as a continuum throughout the DIC-analysis. Negative strains over the mesh were measured along the transverse direction (up to −9% in PMHS #6 with configuration 10x10 + mesh

0x20) highlighting constriction of the mesh along that direction. The use of glue between the mesh and the abdominal wall decreased the amplitude of the strains along this direction. The distribution of the 1-std deviation confidence in the match over the external surface of the abdominal wall was plotted for each configuration at maximum pressure inflation. For all configurations, it was found that values varied between $3x10^{-3}$ and $17x10^{-3}$ pixels. Overall, the regions located at the outskirts of the region of interest exhibited the largest values as well as regions comprising discontinuities along the midline or the edges of the mesh.



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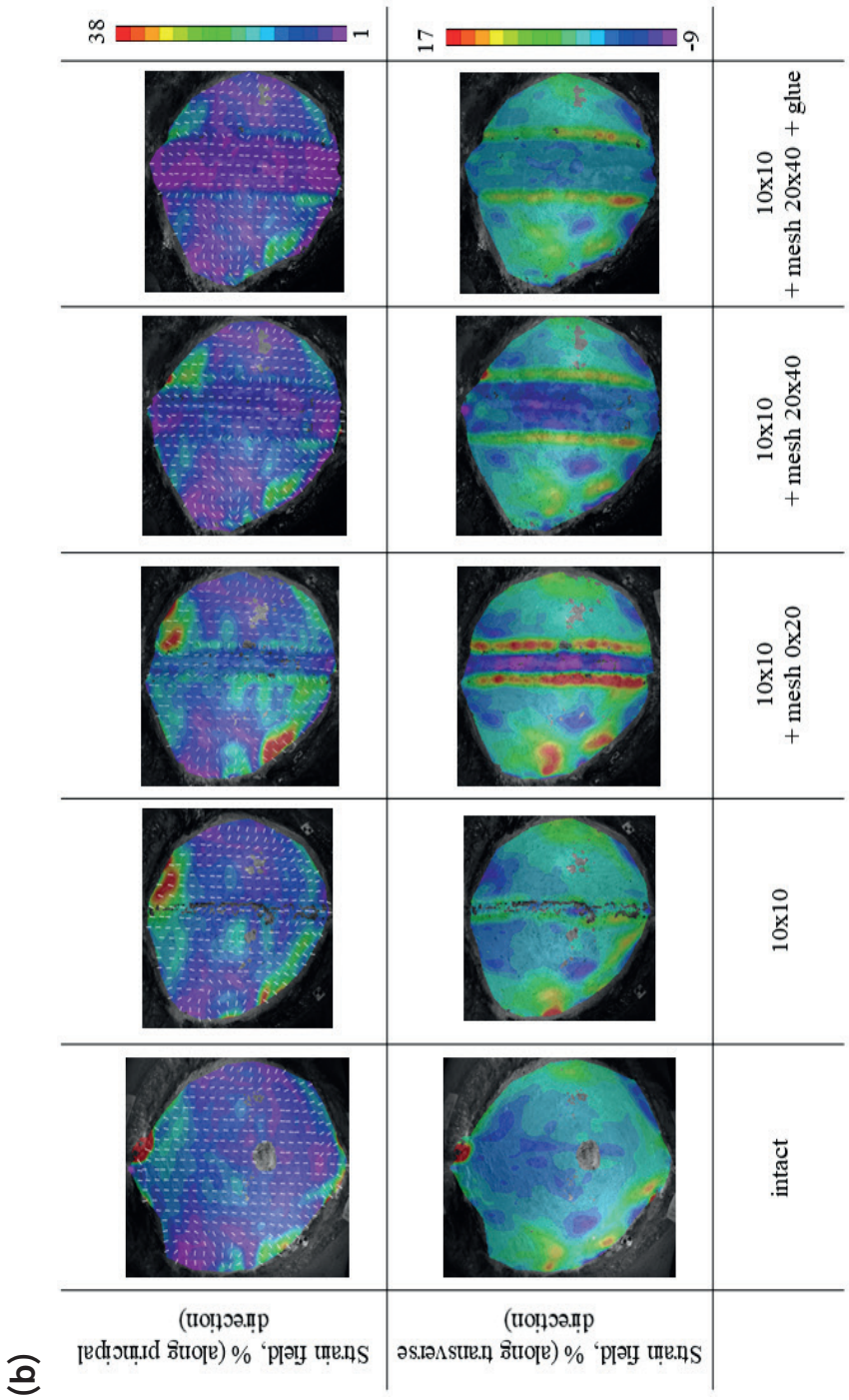

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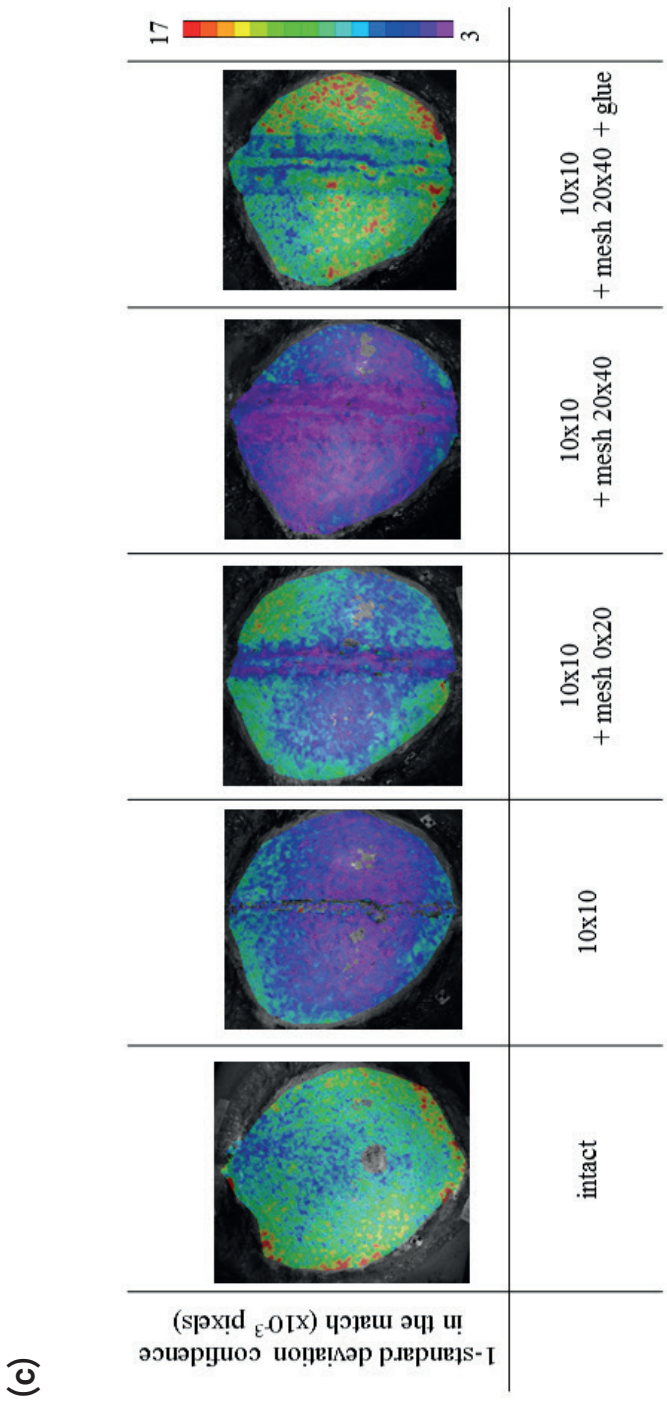

Figure 5. Position, displacement fields (a), strain (Green-Lagrange) fields (b) and 1-std deviation confidence in the match (c) at maximum inflation (35 mmHg) on the external surface of the abdominal wall (PMHS #6). The last test of each configuration is shown.

Displacement along the antero-posterior direction of the point located on the midline 3 cm cranially to the umbilicus was plotted as a function of the pressure for each PMHS and each configuration (Figure 6). This location was chosen as it was observed to experience the highest deflection for each PMHS and each configuration tested. The origin along the antero-posterior direction was set as the position of the marker placed on the table and tracked using Vic-3D. Overall, the shape of the curves looked similar for the four PMHS tested, highlighting a bilinear response. At low values of pressure (<10 mmHg), a relatively rapid increase of the displacement was observed whereas from 10 to 40 mmHg, the slope of the curves was much lower. For each PMHS, the intact configuration led to the highest displacement values. Lower values were observed for the configurations 5x5 and 10x10; although no visible differences were distinguished between these two modalities. Regarding the configurations with the use of mesh reinforcement, a larger mesh overlap would result in a lower displacement in comparison with the intact, 5x5 and 10x10 configurations. The use of glue for mesh fixation led to the lowest values of displacement.

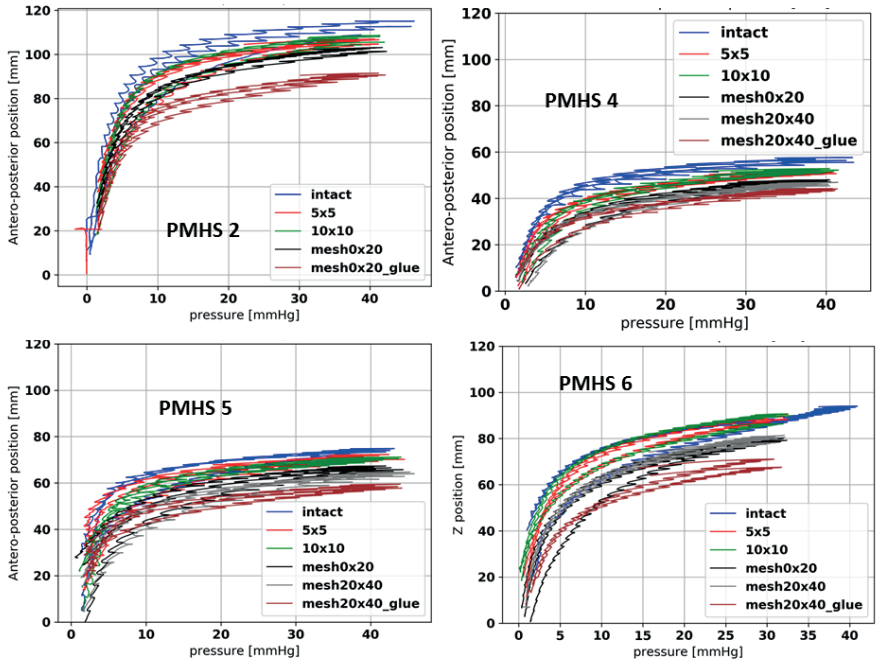

Figure 6. Position along the antero-posterior direction of a point located 3 cm cranially to the umbilicus as function of the pressure.

Profile views of the abdominal wall in the longitudinal and transverse directions for each PMHS and for each configuration are shown in Figure 7. Similar observations were made regarding the amplitude as those made for maximum displacement. However, the shape of the curves was different as a function of the closure configuration was tested. In comparison with the intact configuration, the abdominal wall profiles looked less rounded when a mesh was tested. It should be noted that the peaky part visible for the intact configuration was due to the presence of the umbilicus. No macroscopically visible difference was distinguished between the intact, 5x5 and 10x10 configurations.

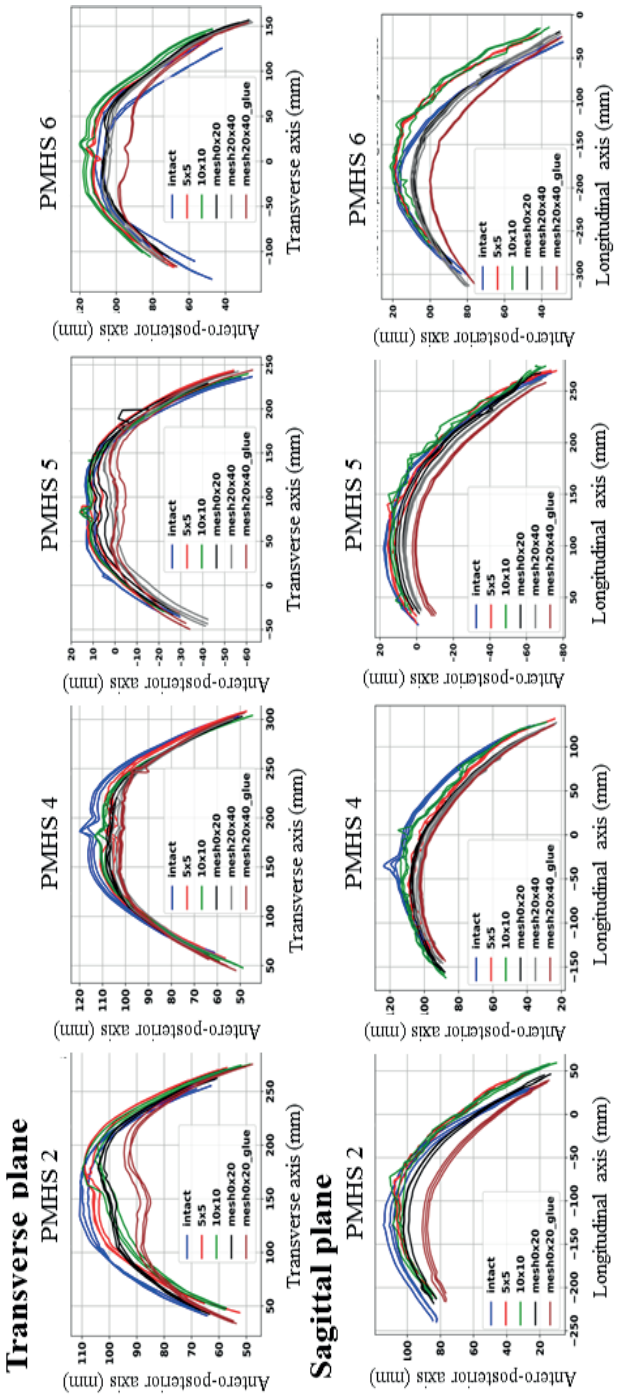

Figure 7. Profile view (in sagittal and transverse plane) of the abdominal wall of each PMHS at maximum deflection (35 mmHg).

Strains in the principal and transverse directions were averaged over the midline (4-cm width rectangle, see Figure 2) and plotted as a function of the pressure for each PMHS and each configuration (Figure 8). The response of the first test of each configuration is plotted using a dashed line. The first test of each configuration exhibited a different response in comparison with the two other consecutive tests, which could be explained by the fact that the first test acted as pre-conditioning. In this respect, non-linearity of pressure-strain response in the principal direction was more marked for the configurations intact, 5x5, 10x10. No visible difference was distinguished between the configurations intact, 5x5 and 10x10. The strain amplitude decreased when a mesh was used. However, differences were observed (lower strain amplitude), when a higher mesh overlap was tested. In this case, differences were more marked in the transverse directions. First, the strain amplitude limited to −5 and 5%. The intact configuration led to very low transverse strain amplitudes whereas the configurations 5x5 and 10x10 led to positive strains highlighting dilatation around the midline along the transverse direction. The use of a mesh led to negative transverse strain highlighting some constriction around the midline in the transverse direction. Finally, the use of glue to simulate the integration process strongly altered the response of the abdominal wall with a quasi-linear pressure-strain response.

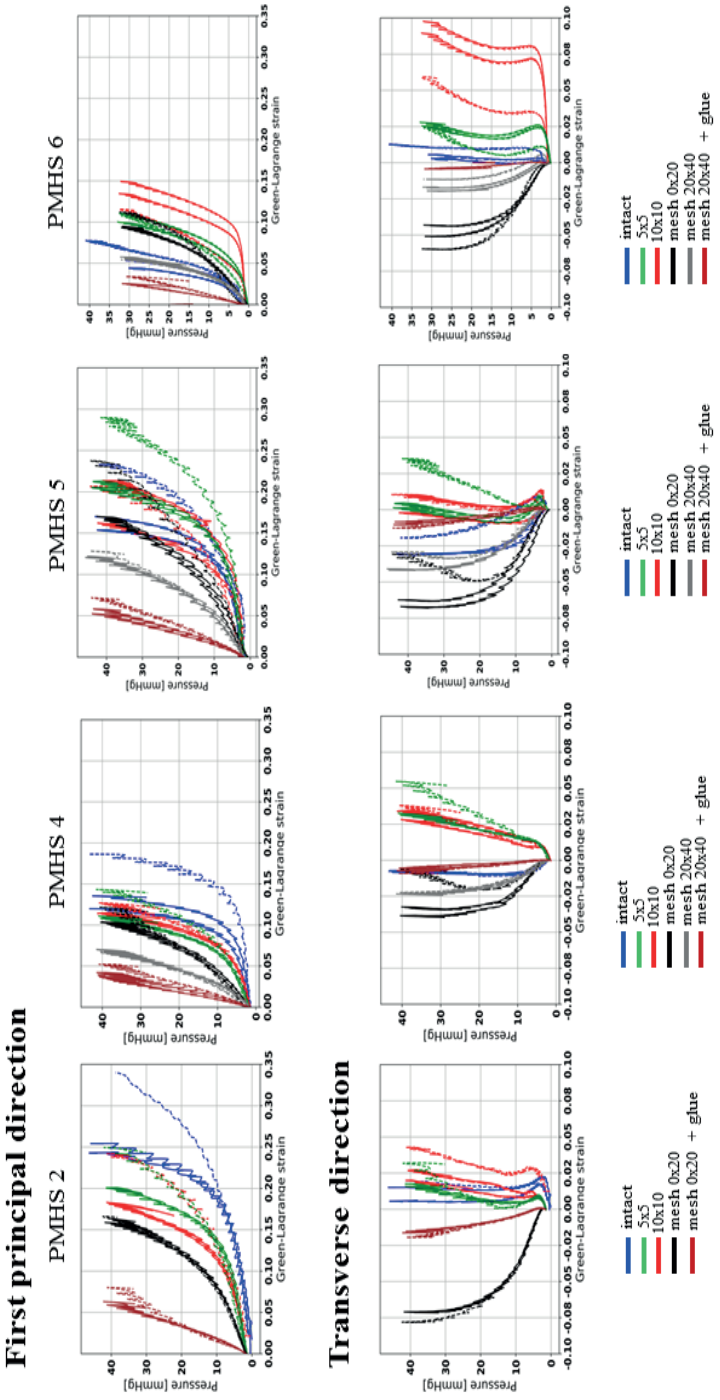

Figure 8. Strains averaged over the midline (rectangle defined in Figure 2) along the first principal (1st line) and the transverse (2nd line) directions for each PMHS as a function of the pressure. The dashed lines correspond to the first test of the configuration considered. line) directions for each PMHS as a function of the pressure. The dashed lines correspond to the first test of the configuration considered.

Discussion

In this present study, four PMHS were tested to study the response of the abdominal wall as a function of five different midline closure configurations, including the use of a mesh, using a DIC-based method. Strain fields were successfully estimated over a region covering the anterior rectus sheath and the external surface of the external oblique muscles. Besides artifacts towards the edges of the region of interest, noise was also visible around the midline and required to be filtered making the analysis difficult over this region.

The displacement of the xiphoid process and the pubic symphysis was tracked as a function of the inflated pressure and was found to be relatively high (up to 50 mm and 30 mm along the antero-posterior direction and the cranio-caudal direction, respectively) despite the use of ratchet straps applied for fixation of each PMHS. *In vivo,* breathing-like activities lead to rib cage motion in directions similar to findings observed in this present study [18]. However, the motion amplitudes observed in this study were much higher for pressure levels comparable to intra-abdominal pressure levels during breathing-like activities (*e.g.* IAP = 20 mmHg measured by Cobb *et al.*) when compared with results from literature (*e.g.* 3.71 mm cranial motion of the sternum measured by De Groote *et al.* during tidal breathing) [18, 19]. This finding could be due to the cranial displacement of the diaphragm during the inflation. Simultaneous inflation the abdominal cavity and the lungs could mitigate this movement and phenomenon by keeping the diaphragm in a more caudal position.

The intact configuration exhibits a highest pole of displacement in comparison with the other configurations in PMHS #2, #4 and #5. PMHS #6 showed opposite results with a highest pole displacement for the repaired configuration using stitches (5x5 and 10x10). The results obtained from PMHS #2, #4 and #5 could be explained by the fact that closing the midline using stitches made the midline region stiffer and even more when an additional mesh was placed. This could explain the lower-amplitude deflections observed for these configurations in comparison with the intact configuration. This could have attributed to the fact that closing the midline with stitches (*e.g.* 10x10 mm) links the two parts of the abdominal wall at 10 mm from the midline, thereby applying a tension to the soft tissue at the same time compressing the tissue

incorporated by the sutures, making the midline region stiffer. However, this phenomenon was not visible for PMHS #6 for unknown reasons. As an assumption, although both height and weight were unknown, the anthropometric dimensions of PMHS #6 suggest that this PMHS had a high BMI and could be considered an outlier. Podwojewski *et al.* presented results showing larger pole displacement for repaired abdominal walls compared to the intact abdominal walls [17]. However, besides the *ex situ* configuration of their experimental setup, the repair configuration consisted of placing a mesh on the incision without closing the *linea alba* which makes comparison with the results derived from this study difficult.

Regarding the strain fields, the first principal direction was found to be oriented in the cranio-caudal direction around the midline for all configurations. This finding could be explained by the boundary conditions applied to the abdominal wall coming from the high-amplitude cranial displacement of the ribcage. Higher amplitude strains were observed over the lateral parts of the abdominal wall in comparison with the anterior rectus sheath region. High-amplitude patterns were visible along the midline when stitches (5x5 and 10x10) were used to close the midline. The strain patterns over the midline were unknown in the configurations with mesh, since the midline was hidden by the textile mesh. However, these high-amplitude patterns observed for the 5x5 and 10x10 configurations might have moved from the midline to the edges of the mesh. The high-amplitude patterns could also be a result of sliding between mesh and the surrounding soft tissue. Also, the amplitude of the strain in the transverse direction was found to be very high for the 5x5 and 10x10 configurations, close to zero for the intact configuration and negative when a mesh was used. Warp knitted textile prosthetic meshes, such as the ones used for this study, exhibit large lateral constriction when subjected to uniaxial tests. The boundary conditions derived from these tests may have placed the mesh in this configuration leading to the observed negative transverse strains. Although the mesh was fixated using stitches along its edges for the configurations mesh 0x20 and 20x40, sliding between the abdominal wall and the mesh may have occurred making the deformation of the mesh along the transverse direction possible between the stitches. This sliding was removed when glue was added between the mesh and the abdominal wall, leading to more limited transverse strains (Figure 5b).

In a clinical study, differences in the occurrence of incisional hernia were found when small bites (*i.e.* 5 mm by 5 mm) in comparison with large bites (*i.e.* 10 mm by 10 mm) were used [5]. No biomechanical difference was highlighted in this study. Multiple reasons could explain this discrepancy with the present findings: first, this experimental protocol might not have been able to detect the specific response of the abdominal wall caused by these two closure configurations. Although DIC-based measurements may provide high resolution, the camera positioning used for this study was set to measure the response of the external surface of the myofascial abdominal wall providing a large enough field of view to track the response of the abdominal wall throughout the whole inflation. This camera positioning may have led to a resolution of the measurements high enough to follow small-amplitude phenomena. Moreover, many discontinuities were present around the midline after closing which makes data filtering in this region necessary. Second, it was found that the PMHS model used in this study led to high-amplitude motion of the ribcage throughout the inflation of the abdominal cavity. These boundary conditions, which were similar for all the configurations tested in this study, might not be representative from physiology considering regular *in vivo* activities (*e.g.* tidal breathing). It should be noted however that this high-amplitude motion of the ribcage may occur in a patient during laparoscopic surgery or deep breathing for example [20]. Ribcage motion more representative of regular *in vivo* activities (*e.g.* tidal breathing) may have led to a different response of the midline that could have been more transversally oriented.

In this study, the response of the abdominal wall was studied when subjected to intra-abdominal pressure up to 40 mmHg. This range includes pressure values measured *in vivo* for some daily activities such as breathing in a standing position (20 mmHg) or Valsalva maneuver (39.7 mmHg) [19]. Other daily activities such as coughing or jumping may lead to intra-abdominal pressure up to 127 and 252 mmHg, respectively [19]. In these present experiments, insufflation pressures did not exceed 40 mmHg to minimize alteration of the soft tissue. During tidal breathing, the diaphragm lowers, decreasing the volume of the abdominal cavity and making the intra-abdominal pressure higher. For activities such as cough or jumping, the muscles of the abdominal wall (rectus abdominis, external and internal oblique, transverse abdominis)

contract, leading to the high intra-abdominal pressure values mentioned. The passive *post mortem* design of these experiments in comparison with the *in vivo* or clinical study performed might explain these discrepancies in results. Third, these tests simulated the response of the abdominal wall just after surgery as most incisional hernias tend to develop in an early stage. However, clinical outcomes might not only be driven by the initial conditions derived from the midline closure but rather to biological responses including the generation of new tissue during the healing process. As a perspective, it would be interesting to conduct an *in vivo* animal study to study whether differences could be highlighted as a function of time.

It was found that the strain amplitude and the maximum displacement decreased when a mesh as a suture line reinforcement was used. These findings were amplified when a larger overlap was used. The impact of the mesh and its overlap was studied for the onlay configuration only. As a speculation, it would be interesting to compare the results obtained with other configurations such as retromuscular or preperitoneal. This point will be further investigated.

Cyanoacrylate glue was used to mimic tissue integration by attempting to tie the mesh to the surrounding soft tissue. This glue resulted in a decrease of the strain fields around the midline combined with a linear strain-pressure response. However, these results have to be considered carefully as the use of such glue could alter the mechanical intrinsic parameters of the mesh and also the surrounding tissue. It was not demonstrated that the use of cyanoacrylate glue accurately mimics tissue integration as it would naturally occur during the healing process [21, 22].

The order of testing these six configurations was the same for every PMHS. This could have influenced the results of the later configurations, as the abdominal wall would have been subjected to repeated inflation and deflation already. However, results of PMHS #1 (control) showed that the strain field varied little as the number of pressure cycles increased, although a stiffening effect was visible between the first and the last test. Several explanations can be formulated to explain these observations. First, this stiffening could be due to the paint applied before the first cycle that dried as pressure cycles were applied resulting in a stiff layer covering the soft tissue underneath.

Second, stiffening of tissue under cyclic loading is counter to what is typically observed: tissue outside of the measured area may have been recruited to carry some of the load. Additionally, tissue in the unmeasured portion of the volume that contained the pressure, including organs in the abdominal cavity or deep organs, were compressed and underwent stress relaxation or displacement, which may have reduced the overall strain measured in the region of interest. It should be noted that for all other PMHS, the paint was carefully removed and the tissue hydrated at the end of each test. This probably enabled mitigation of the stiffening effect visible for PMHS #1. Furthermore, the effect of the paint, even just after application, is unknown.

When closing the midline, the needle created micro-damage to the soft tissue at each crossing point. Although this damage is part of the modality process, its effect on the next modalities tested is unknown and could alter the response of the abdominal wall. However, the tissue area damaged by the closure process for a given test was either included within the suture loop deriving from to the closure process or located under the mesh when one was used, probably decreasing its impact on the response of the abdominal wall. Two factors not included in this study are suture tension and knot tightness. High suture tension or knot tightness could lead to increased micro-damage, constriction and eventually worsening vascularization, causing ischemia and necrosis. It has been suggested that the use of small bites provides a better distribution of suture tension across the wound, thus lowering the occurrence of the before mentioned negative consequences, with the final outcome being the occurrence of an incisional hernia. Also, there are many different areas (*i.e.* directly around the suture and away from the suture) with different mechanical environments and responses. Perfusion and ischemia should be always considered in relation to the observed stress level of one specific area. Additionally, an equal distribution of forces is needed in order to achieve the optimal ratio of collagen type 1 to collagen type 3 [5]. Suture tension and knot tightness are thought to be contributing factors to the formation of incisional hernia. Devices to measure these factors are being created and future research should include measurements with these devices.

This study has focused on the response of the midline as a function of the closure configuration used and the use of a mesh as reinforcement. The data

provided in this study cover the whole abdominal region including the external surface of the external oblique muscles. Within the context of numerical model development, the data provided within this study could be used to calibrate or evaluate the response of such models.

Conclusion

A digital image correlation-based method was developed to study the impact of different closure configurations and the use of a mesh as suture line reinforcement on the response of the abdominal wall, in particular within tissues surrounding the midline in PMHS. Two closure modalities (5x5 and 10x10 mm) that were found to lead to different clinical results were considered. Additionally, the impact of an onlay mesh with overlap was studied. No visible differences were observed between the 5x5 and 10x10 closure configurations. Possible reasons could be the lack of relevance regarding physiology of the PMHS model used for this study (*e.g.* lateral muscle contraction was not simulated, boundary conditions were not relevant with regard to the most regular activities such as tidal breathing), the scale at which differences could be highlighted between these two modalities and the absence of impact of the initial conditions in comparison with higher-order biological responses occurring during the healing process. The use of a mesh as a suture line reinforcement highlighted stiffer behavior of the midline area for similar intra-abdominal pressures, which was amplified when a larger overlap was used. High-amplitude strain patterns observed when only stitches were used (*e.g.* 10x10) seemed to move from the midline area to the lateral parts of the mesh when a prosthetic mesh was tested. The next step should be to investigate the mesh location (*e.g.* retromuscular) and additional time points to better account also for the healing process *in vivo*.

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Chapter 3

Evaluation of a new suture material (Duramesh™) by measuring suture tension in small and large bites techniques for laparotomy closure in a porcine model

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Y. Yurtkap and F.P.J. den Hartog contributed equally to this work.

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Abstract

Purpose

After closure of laparotomies, sutures may pull through tissue due to too high intra-abdominal pressure or suture tension, resulting in burst abdomen and incisional hernia. The objective of this study was to measure the suture tension in small and large bites with a new suture material.

Methods

Closure of the *linea alba* was performed with small bites (i.e., 5 mm between two consecutive stitches and 5 mm distance from the incision) and large bites (i.e., 10 mm × 10 mm) with Duramesh™ size 0 (2 mm) and PDS II 2-0 in 24 experiments on six porcine abdominal walls. The abdominal wall was fixated on an artificial computer-controlled insufflatable abdomen, known as the 'AbdoMan'. A custom-made suture tension sensor was placed in the middle of the incision.

Results

The suture tension was significantly lower with the small bites technique and Duramesh™ when compared with large bites (small bites 0.12 N (IQR 0.07–0.19) vs. large bites 0.57 N (IQR 0.23–0.92), $p < 0.025$). This significant difference was also found in favour of the small bites with PDS II 2-0 ($p < 0.038$). No macroscopic tissue failure was seen during or after the experiments.

Conclusion

Closure of the abdominal wall with the small bites technique and Duramesh™ was more efficient in dividing suture tension across the incision when compared to large bites. However, suture tension compared to a conventional suture material was not significantly different, contradicting an advantage of the new suture material in the prevention of burst abdomen and incisional hernia during the acute, postoperative phase.

Introduction

Abdominal wound dehiscence (burst abdomen, 'Platzbauch') has an incidence of up to 4% and it is a feared early complication after abdominal surgery with sequelae like evisceration, prolonged hospitalization and high mortality rates [1]. In addition, incisional hernia is a common complication after midline incisions with a 5–30% incidence and may result in pain, reduced quality of life and high healthcare costs [2-4].

Several suture materials and techniques for the closure of the *linea alba* after midline incisions have been investigated, however, there is still a need for closure techniques that can prevent incisional hernia [5]. The current recommendation, also stemming from a recent randomized controlled trial, is to use the small bites technique (i.e., 5 millimetre (mm) tissue bites and 5 mm between two sutures) with slowly absorbable suture materials for the closure of the *linea alba* after midline laparotomy [6]. Nevertheless, this randomized controlled trial showed that the occurrence of an incisional hernia still persists in 13% after a 1-year follow-up [6]. This result confirms that the exact biomechanical basis underlying the superiority of the small bites technique remains unknown.

In a rodent model, the dynamic change of the surgical suture tension has been investigated with the use of a customised force sensor [7]. The development of a comparable suture force or tension sensor permitted researchers and surgeons to gather data on suture tension in various tissues, suture materials, suturing patterns and closure techniques. A suture may pull through tissue due to localized pressure or tension which may cut through tissue immediately resulting in a burst abdomen or an incisional hernia after a period of time from disturbed healing by infection and/or tissue necrosis Dumanian and colleagues created a novel suture of uncoated mid-weight macroporous polypropylene mesh - named Duramesh™ suturable mesh suture - to reduce the occurrence of sutures pulling through tissue and to prevent incisional hernia formation [8].

The aim of this study was therefore to measure suture tension using the small bites technique and the newly developed Duramesh™ size 0 (2 mm) also in comparison with the large bites technique, by using an implantable suture

tension sensor which was developed specifically for these experiments. Furthermore, the small and large bites techniques were compared with a conventional suture material, *i.e.,* PDS II 2-0, as a control suture material. All experiments were performed in an ex vivo porcine abdominal wall using the artificial 'AbdoMan'.

Methods

Suture tension sensor

An implantable suture tension sensor was developed using a Force Sensing Resistor (Interlink Electronics FSR 400, Interlink Electronics, Westlake Village, CA, USA) with an actuation force of approximately 0.2–20 N [10]. A three-dimensional (3D) model was developed for the enclosure of the suture tension sensor (Figure 1a). The tension generated by the suture in the actuator notch is translated downward onto a circular surface, precisely and evenly pressing down on a force sensor within the suture tension sensor (Figure 1b and 1c). An analog-to-digital converter (ADC) and an Arduino Uno controller (Arduino AG, Somerville, MA, USA) were used to read the raw output from the suture tension sensor. A custom-made program was written to create a live graph of the tension sensor data in Newtons (N).

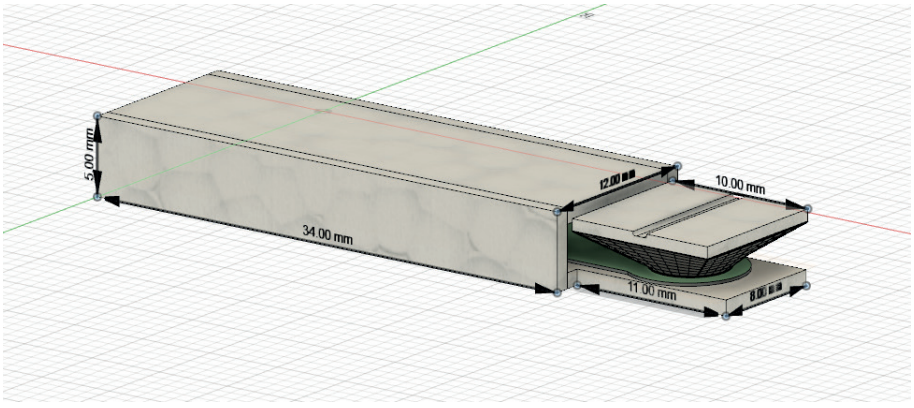

Figure 1a. Complete sensor enclosure and Interlink Electronics FSR 400 (in green). Total probe dimensions: 45 mm × 12 mm × 5 mm.

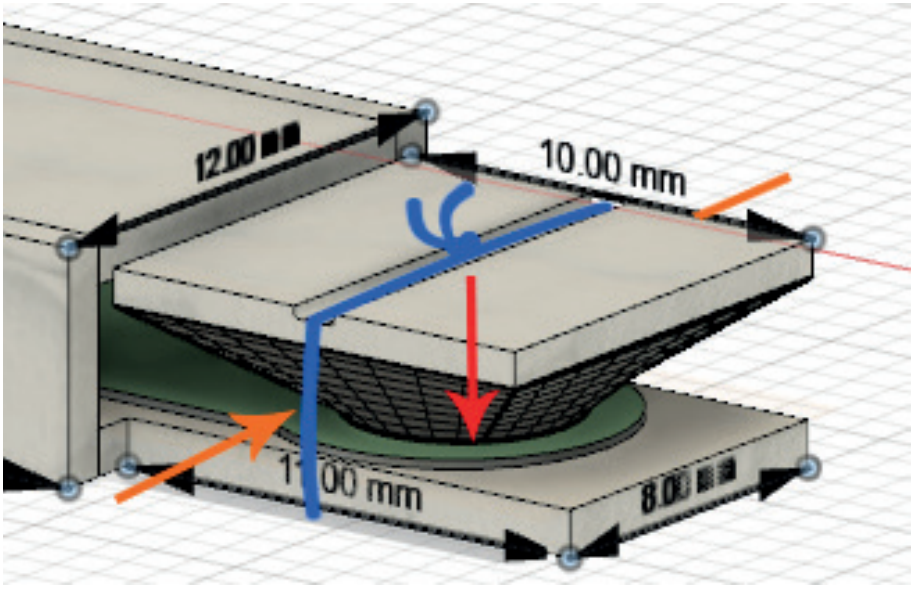

Figure 1b. The tension in the suture (orange arrows) is translated to a downward force, applied to the suture tension sensor (red arrow).

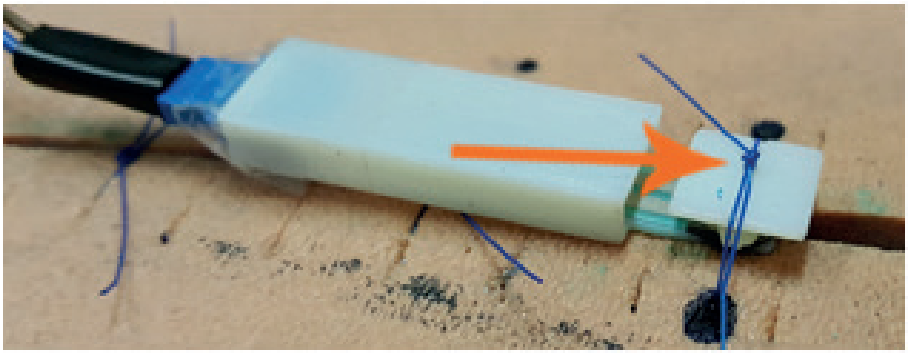

Figure 1c. The suture tension sensor in an experimental set-up with an artificial abdominal wall and PDS-II 2-0 single suture. The tension in the suture marked by the orange arrow was measured.

Measuring model

The 'AbdoMan' was developed as an artificial simulation of the human abdominal wall by taking the muscle contractions and intra-abdominal pressure into account [11]. In these current experiments, only the intra-abdominal pressure was considered. A 3500 ml air-filled collecting bag was placed on a three-dimensional printed part in the shape of an abdominal wall. A laparoscopic insufflator (Olympus UHI-3 High Flow Insufflator, Olympus Corporation, Shinjuku, Japan) was used to apply insufflation pressures up to 20 millimetres of mercury (mmHg). After sensor placement and prior to insufflation, a baseline suture tension was measured over the course of one minute. Validation of the suture tension sensor was performed before these experiments, by varying the force applied to the suture tension sensor in a controlled manner, verifying whether the suture tension sensor would be able to correctly detect and measure these variations. The measured suture tension is relative to the baseline tension in the closed incision. The measurements are a derivative of the actual tension within the suture.

Duramesh™

Duramesh™ is a novel suturing concept, based on the principles of meshes, used in hernia repair, while providing the precision and flexibility of a suture [12]. It is a non-resorbable suture, made of polypropylene. The three-dimensional macroporous structure has a larger surface than standard sutures and it has been shown to stimulate better tissue integration in an in vivo porcine model [12].

Experimental set-up

Six porcine abdominal walls of female Yorkshire-Landrace pigs with comparable dimensions, ranging in weight from 30 to 40 kilograms (kg) were explanted directly after euthanasia and frozen at −20 Celcius (°C). Twenty-four hours prior to the experiments, the abdominal wall was thawed [13]. Two midline incisions of 5 cm each (*i.e.,* cranial and caudal) were made through all layers of the abdominal wall. This number of midline incisions and their length was chosen, because this length would be the longest possible length

compatible with all specimens. The abdominal wall was inversely placed with the peritoneum upwards and fixated onto the 'AbdoMan' (Figure 2). The *linea alba* was closed with continuous sutures including all layers of the abdominal wall, including the peritoneum. Closure was performed using the small bites (*i.e.,* 5 mm between two consecutive stitches and 5 mm distance from the incision) and the large bites (*i.e.,* 10 mm between two consecutive stitches and 10 mm distance from the incision) techniques with Duramesh™ size 0, 2 mm (Duramesh™ Suturable Mesh, Inc., Dorado, Puerto Rico, USA) and PDS II 2-0 (Ethicon, Somerville, NJ, USA). Locations (*i.e.,* cranial and caudal) were switched for small and large bites to randomize for location. Each experiment was repeated twice, using the existing incisions. The suture tension sensor was placed in the middle of the incision. All experiments were performed by a single researcher. Lastly, the collecting bag was insufflated to 20 mmHg for a duration of 30 minutes (min).

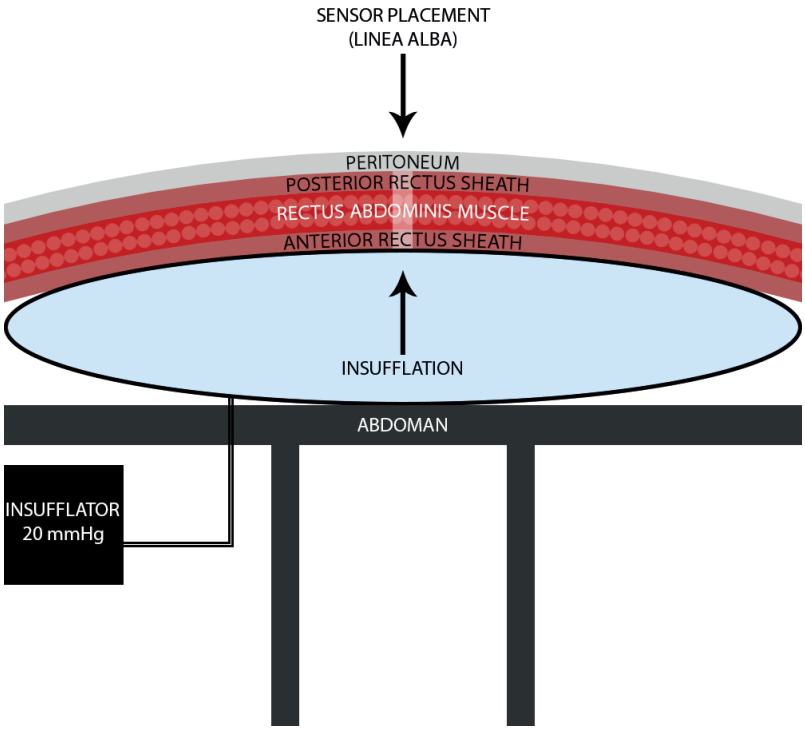

Figure 2. Experimental set-up.

Finally, the suture tension was compared between:

1. Small bites with Duramesh™ size 0 versus large bites with Duramesh™ size 0 ($N = 12$).
2. Small bites with PDS II 2-0 versus large bites with PDS II 2-0 ($N = 12$).
3. Small bites versus large bites with both materials.
4. Small bites with PDS II 2-0 versus small bites with Duramesh™ size 0.
5. Large bites with PDS II 2-0 versus large bites with Duramesh™ size 0.

Data analyses

Results are presented as median differences and interquartile ranges in suture tension. Statistical significance was assessed using a Wilcoxon rank-sum test for all samples comparing two different modalities (*i.e.,* small bites, large bites, Duramesh™ size 0, and PDS II 2-0) after 25 min. p values lower than 0.05 were considered statistically significant. Python for Windows, version 3.5.1. (Python Software Foundation, Beaverton, USA) was used to perform all statistical analyses.

Results

In total, 24 experiments were performed. No macroscopic tissue failure was visible during or after the experiments. Median suture tension was calculated for one point in time; i.e., at 25 min from the start of insufflation, when the suture tension had reached a plateau in all experiments. When considering the two suture materials individually, each showed a significant difference in suture tension between small and large bites, in favour of the small bites. Regarding Duramesh™ size 0: small bites 0.12 N (IQR 0.07–0.19) versus large bites 0.57 N (IQR 0.23–0.92), $p < 0.025$ (Figure 3). Regarding PDS II 2-0: small bites 0.15 N (IQR 0.05–0.31) versus large bites 0.56 N (IQR 0.37–0.98), $p < 0.038$ (Figure 4).

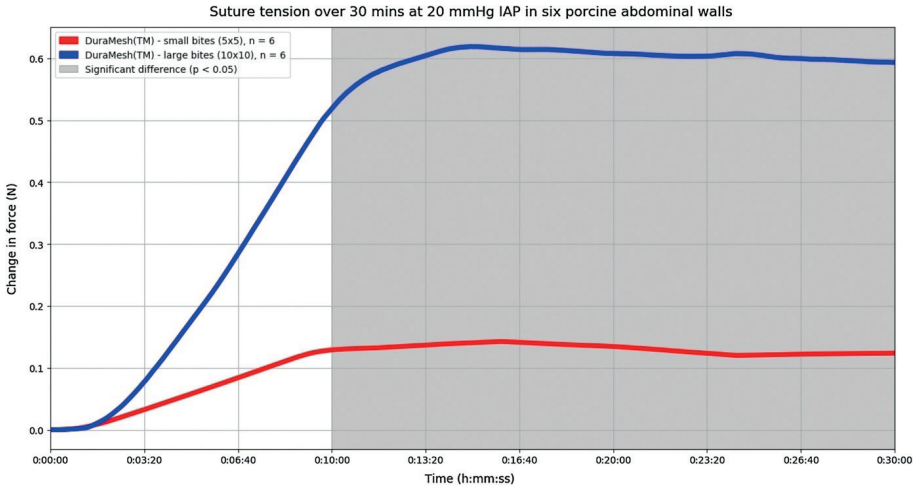

Figure 3. Experiments performed with only Duramesh™ size 0. The median change in suture tension of all small bites is shown by the red line. The median change in suture tension of all large bites is shown by the blue line. Small bites were significantly more efficient in dividing suture tension across the incision when compared to large bites at time points in the shaded area.

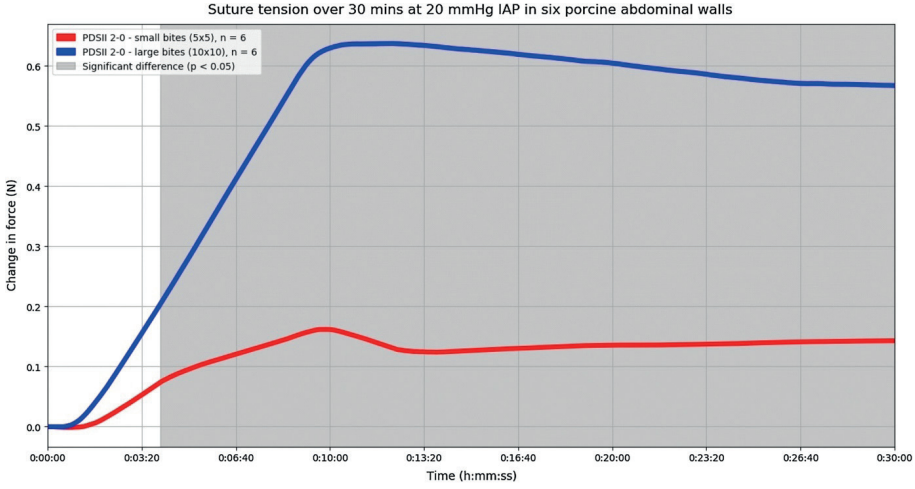

Figure 4. Experiments performed with only PDS II 2-0. The mean change in suture tension of all small bites in red. The mean change in suture tension of all large bites in blue. Small bites were significantly more efficient in dividing suture tension across the incision when compared to large bites, at time points in the shaded area.

Irrespective of the suture material used, the tension in the sutures was significantly lower when the *linea alba* had been closed with small bites when compared to the tension in the sutures when large bites had been applied (small bites 0.14 N (IQR 0.06–0.20) versus large bites 0.56 N (IQR 0.31–0.98), $p < 0.0015$, Figure 5).

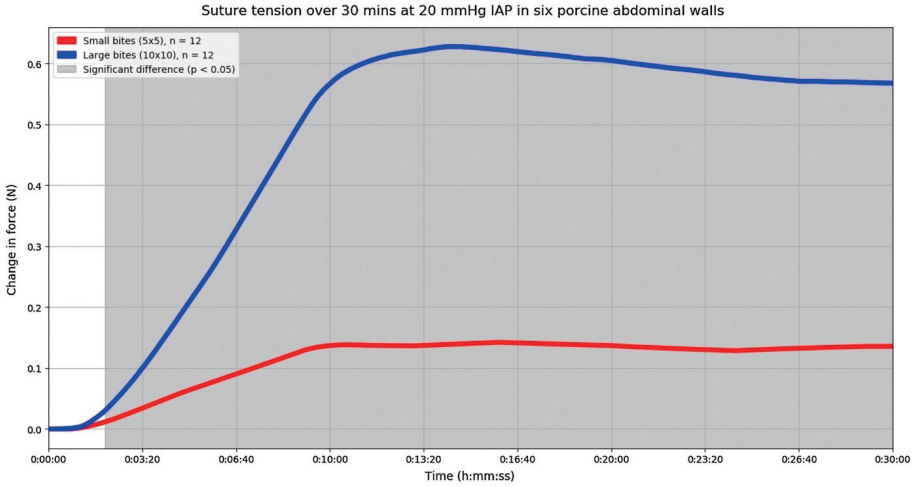

Figure 5. Experiments performed with both suture materials. The median change in suture tension of all small bites is shown in red. The median change in suture tension of all large bites is shown in blue. Small bites were significantly more efficient in dividing suture tension across the incision when compared to large bites, at time points in the shaded area.

When only considering small bites, there was no significant difference in suture tension between Duramesh™ size 0 and PDS II 2-0 (Duramesh™ size 0 0.12 N (IQR 0.07–0.19) versus PDS II 2-0 0.15 N (IQR 0.05–0.31), $p > 0.05$, Supplemental Figure 1). Similarly, when only considering large bites, there was no significant difference in suture tension between Duramesh™ size 0 and PDS II 2-0 (Duramesh™ size 0 0.57 N (IQR 0.23–0.92) versus PDS II 2-0 0.56 N (IQR 0.37–0.98), $p > 0.05$, Supplemental Figure 2).

Discussion

In this present study, small bites and the use of Duramesh™ resulted in a significantly lower suture tension when compared to the tension in the sutures in large bites in a porcine abdominal wall. The suture tension was measured with a custom-made suture tension sensor in an experimental set-up using the artificial 'AbdoMan'. This significant difference was also found when the same

comparison was made with the use of PDS II 2-0 as a control suture material. These findings were analogous to findings from a recent clinical study [6]. The superiority of the small bites technique is not limited to PDS II 2-0 sutures, but also holds for suture materials with an elaborate three-dimensional structure, such as the Duramesh™ size 0 and perhaps for other types of suture materials. However, in this present experiment Duramesh™ size 0 was neither superior, nor inferior, compared to PDS II 2-0. This finding makes Duramesh™ a viable option in choosing suture materials for abdominal wall closure. Nevertheless, most previous experiments with Duramesh™ have revolved around linearly pulling it until either tissue or suture failure [12, 14]. In this experimental set-up, Duramesh™ was tested to much weaker forces i.e., 20 mmHg. Simulating pulling to failure in this set-up would involve raising the intra-abdominal pressure to (much) higher levels than 20 mmHg, perhaps ranging in the hundreds of mmHg. Therefore, a tensile test would be more suitable for this kind of experiments to demonstrate a difference. When being pulled, the Duramesh™ size 0 stretched and flattened like a ribbon, which may be helpful in dividing the suture tension across the wound. When the Duramesh™ size 0 was pulled through the tissue, the structure of the suture was occasionally damaged. This damage may have compromised the integrity of its shape, thereby impairing its mechanism of action. That being said, the Duramesh™ size 0 or PDS II 2-0 never broke completely. It should be noted that only size 0 (2 mm) of the Duramesh™ was tested in these present experiments. The expectation is that the superiority of Duramesh™ will be clearer in an in vivo model, where tissue integration can be measured as well.

The relation between suture material and the development of burst abdomen has not been studied extensively. Van Ramshorst et al. found that failure of the knot was a significant cause in addition to other causes like ileus [1]. On the contrary, the effects of different suture materials, suture configurations and suture length to wound length ratio on the occurrence of incisional hernia have been extensively studied [5, 15]. Cooney et al. found the best performing bite separation and bite width to be 5 and 16 mm, respectively, in a biomechanical abdominal wall model [16]. As they also state, this is partly in agreement with the findings of the STITCH-trial. However, they suggest that perhaps a small bite separation should be combined with a large bite depth rather than

a small bite depth like the 5 mm used in the STITCH-trial. Comparing these two modalities should be the next step in this present experimental setup. However, the optimal suture tension has not been studied largely [7]. The tension in a suture is the composite result of the type or resistance of tissue, the suture material used, the force applied by the surgeon during knotting, and the bite width and separation [7]. Proper closure of the abdominal wall involves the close approximation of tissue edges with sutures. If the sutures are too loose, however, the wound edges cannot be properly approximated and there will exist a risk for impaired healing and wound dehiscence. This theoretically would result in an increased risk for incisional hernia formation [1]. Another reason for insufficient suture tension could be the phenomenon of creep, in which the suture will be irreversibly elongated over time as a result of a continuous pulling force [10]. Inadequate abdominal fascial closure may also be seen in cases where the tension in the sutures is too high. The suture may cut through tissue and cause additional tissue damage, tissue necrosis or an incisional hernia [1]. This implies that the relation between suture tension and outcome is parabolic, allowing for the definition of a possibly optimal suture tension [17]. Nonetheless, it is not easy to obtain the ideal suture tension since this is subject to inter- and intra-surgeon variability [18]. It would be helpful to have a device attached to the suture needle or the suture material continuously measuring suture tension so that the surgeon would be able to apply the same suture tension with every knot or throw. While there is no currently available method to determine suture tension during suturing, the pore size of the Duramesh™ was macroscopically changed with higher tension, giving the surgeon feedback while suturing.

As almost in every in vitro study, this study also has limitations. One limitation in this study is the use of porcine abdominal walls instead of human abdominal walls, which were not available. However, in a recently published study, porcine tissue was demonstrated to be an appropriate surrogate for examining the human abdominal wall when it comes to the *linea alba* [19]. Another limitation was that the suture length to wound length ratio of at least 4:1 was established prior to the experiment. However, with the small bites technique, twice as many suture loops were placed than with the large bites technique. The present ex vivo experiments can be considered an acute postoperative

model rather than a wound healing model. As a consequence, it can be concluded that the new Duramesh™ size 0 suture seems to behave similar to a conventional suture like PDS II 2-0, that the advantages of small bite closure of the *linea alba* also apply to it, but that it cannot be expected to prevent the early development of burst abdomen and incisional hernia in a better way. One could propose that the three-dimensional, macroporous structure of the Duramesh™ would provide for a more profound tissue integration, allowing the tissue to grow through its individual threads and completely envelop the suture. This could hypothetically strengthen the wound healing and help prevent incisional hernia, something which has already been shown in in vivo experiments [8]. Finding a way to simulate wound healing, such as in animal models, would allow to focus on incisional hernia formation at a later point in time—after closure of the abdominal wall and during the healing process. In such an experimental setup the Duramesh™ would be expected to be more efficient when compared with conventional suture materials. In the future, this experimental setup and the suture tension sensor might be used for experiments with other suture materials and configurations.

Conclusion

The suture tension with the small bites technique and the use of Duramesh™ size 0 was significantly lower when compared with large bites in this model. Additionally, macroscopic tissue failure was not seen in either suture material during or after the experiment. Further research should be conducted to find out whether these findings are also valid in different stages of wound healing and in abdominal walls of different origins, shapes and sizes, as well as with the use of other types of sutures or suturing techniques.

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Supplemental materials

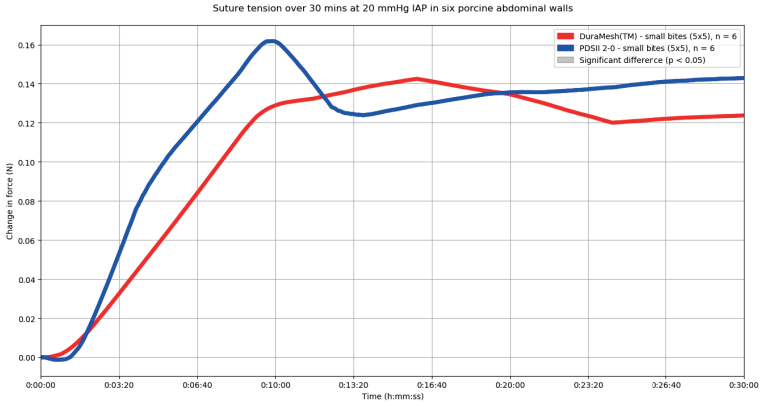

Figure 1. No significant difference in suture tension between Duramesh™ size 0 and PDS II 2-0 was seen when only considering small bites.

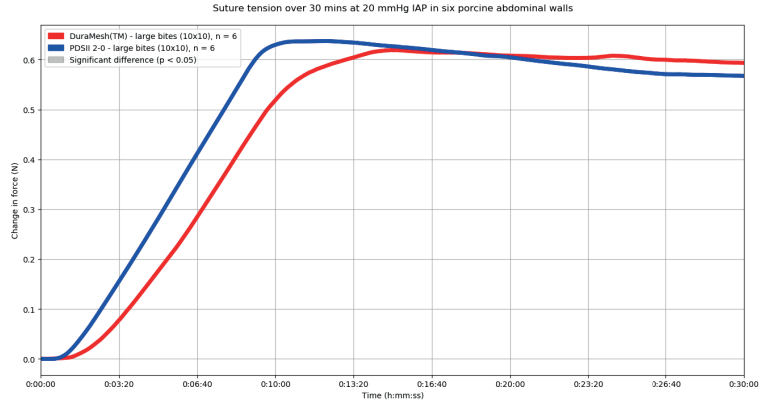

Figure 2. No significant difference in suture tension was seen between Duramesh™ size 0 and PDS II 2-0 when only considering large bites.

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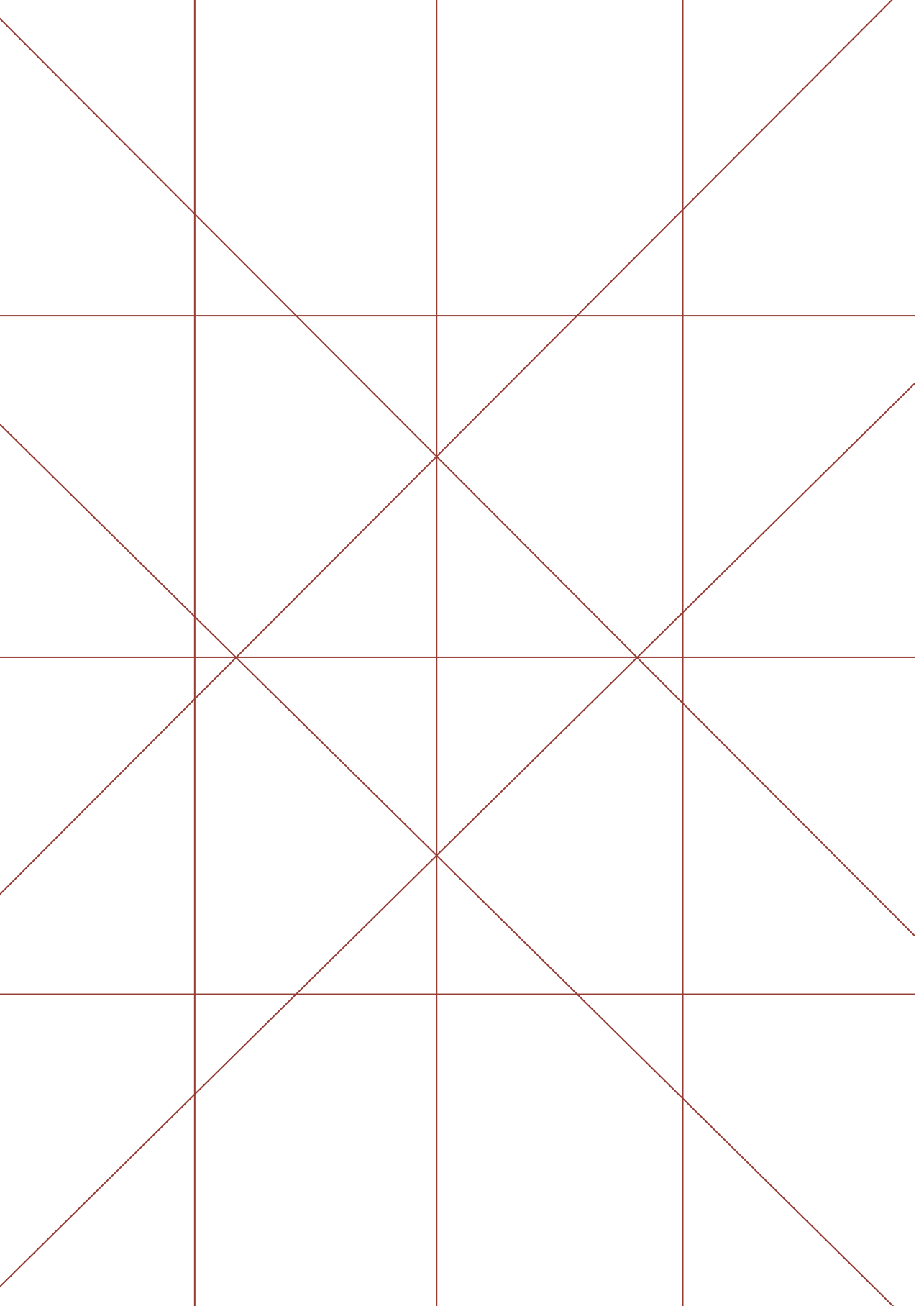
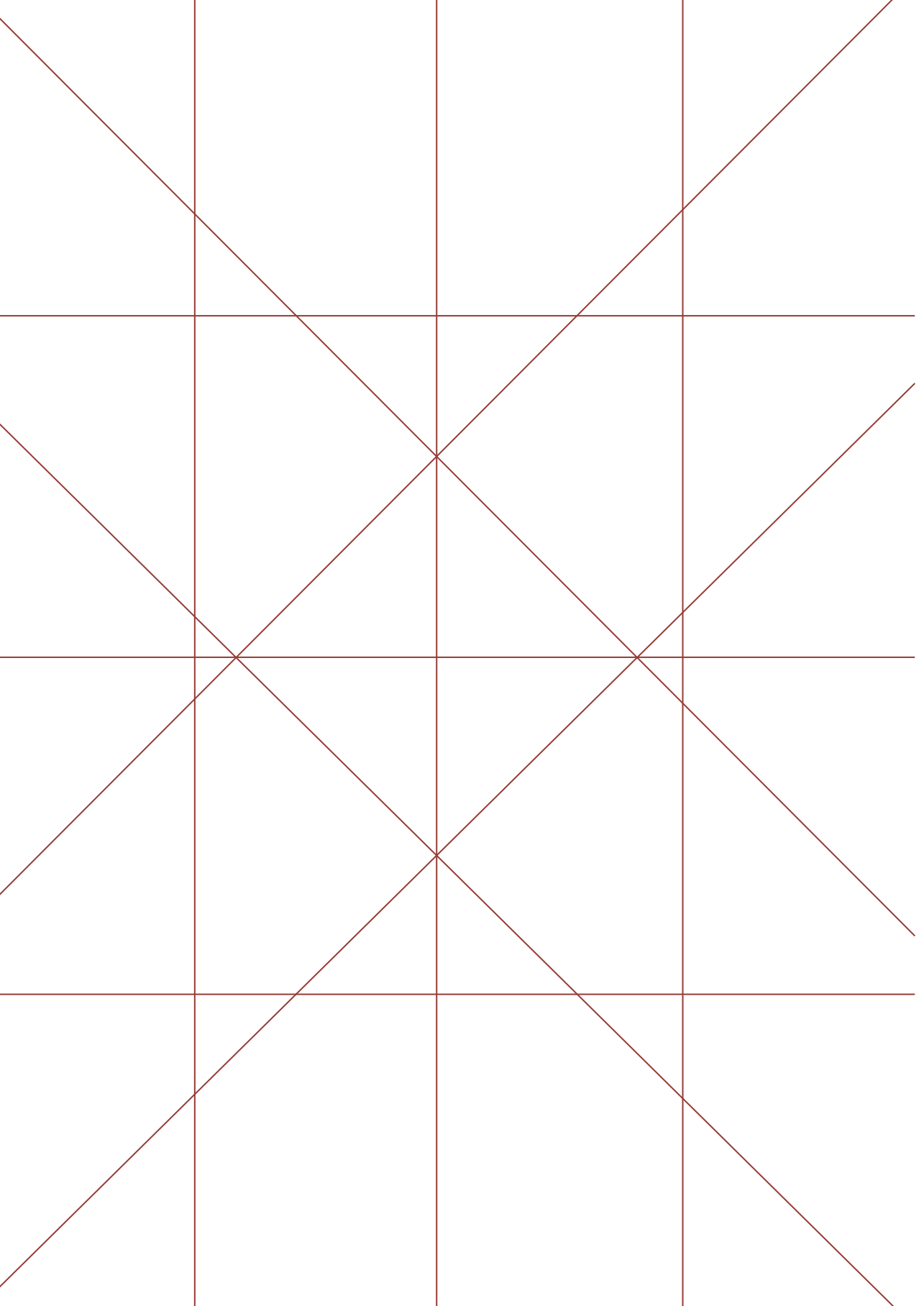


Part II

Fundamental Knowledge in Treatment of Complex Abdominal Wall Hernias



Chapter 4

Anatomical study comparing medialization after Rives-Stoppa, anterior component separation, and posterior component separation

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Abstract

Background

Large incisional hernias require medialization of the *rectus abdominis* muscles to facilitate tension-free closure. Medialization may be achieved by Rives-Stoppa, anterior component separation, or posterior component separation. This study aims to compare medialization achieved by these techniques in postmortem human specimens.

Methods

First, the Rives-Stoppa procedure was performed. Subsequently, anterior and posterior component separation were performed on one side in each specimen, with each specimen functioning as its own control. Medialization was measured at three levels of the *linea alba* with three 1-kg weights. Both medialization obtained in addition to initial medialization after opening the linea alba and total medialization were measured. Results are presented as median and interquartile range.

Results

A total of 13 postmortem human specimens were included (Rives-Stoppa $n = 13$, component separation $n = 10$). Additional medialization after Rives-Stoppa was 1.2 cm (IQR: 0.3–2.2) for the anterior rectus sheath and 2.2 cm (IQR: 1.6–3.0) for the posterior rectus sheath (total medialization: 3.9 and 4.5 cm). For the anterior rectus sheath, additional medialization was 2.6 cm (IQR: 1.2–3.6) after anterior component separation and 1.9 cm (IQR: 0.4–3.4) after posterior component separation ($P = .125$, total medialization: 6.5 and 5.7 cm). For the posterior rectus sheath, additional medialization was 3.0 cm (IQR: 2.2–3.7) after anterior component separation and 5.2 cm (IQR: 4.2–5.9) after posterior component separation ($P < .001$, total medialization: 5.8 and 9.4 cm).

Conclusion

Posterior component separation yielded significantly more medialization of the posterior rectus sheath compared with Rives-Stoppa and anterior component

separation. Anterior component separation may provide marginally more medialization of the anterior rectus sheath.

Introduction

Incisional hernia (IH) remains a prevalent complication after abdominal surgery. The prevalence of IH ranges between 10% and 20% in the general patient population and may be well over 30% in high-risk patients [1-3]. Moreover, recurrence rates after IH repair may be up to 37% [4]. Therefore, IHs remain a surgical challenge and results in approximately 350,000 surgical procedures per year in the United States alone [5].

IHs are associated with (severe) physical and aesthetic complaints [6, 7]. In addition, repair of large and complex IHs is associated with high morbidity and recurrence rates [6, 8-12]. Today, the objective of IH repair is tension-free fascial closure with mesh augmentation [11-14]. To achieve tension-free closure in wide IHs, additional medialization of the rectus abdominis muscles is required. A well-known technique to obtain medialization is the Rives-Stoppa procedure [15, 16]. However, medialization achieved by this technique can be insufficient to close large defects. Therefore, component separation techniques may be used to obtain additional medialization [17-19].

Two regularly applied component separation techniques are anterior and posterior component separation. The anterior component separation was first described by Ramirez *et al.* [19] in 1990. The more recently developed posterior component separation or transverse abdominis release (TAR) was first described by Novitsky *et al.* [18] in 2012. Both techniques are regularly performed to repair large IHs [6, 17, 20]. However, data on the exact medialization potencies of these techniques is lacking. The total medialization distance that can potentially be achieved is vital to estimate the IH defect size that can be closed by a certain medialization technique. To date, no study has compared medialization obtained after anterior and posterior component separation techniques.

The extent of total medialization achieved is less suitable to compare different techniques in an experimental setting because it can be influenced by individual patient factors and might differ slightly between the abdominal sides [21].

Therefore, we propose to use the extent of medialization achieved in addition to the initial medialization after opening the *linea alba.*

The objective of this study was to assess and compare medialization after Rives-Stoppa, anterior component separation, and posterior component separation in postmortem human specimens. The primary outcome measurement was the medialization achieved after Rives-Stoppa, anterior component separation, and posterior component separation in addition to the initial medialization after opening the linea alba. Secondary outcomes comprise total medialization after these three techniques.

Methods

Fresh frozen postmortem human specimens were included. All included postmortem human specimens had consented to tissue donation for scientific purposes. We did not have access to the medical history of the included specimens for this study because of Dutch and European regulations. Specimens with visible or palpable abdominal wall morbidity (*eg*, herniations) or previous surgery that might compromise measurements were excluded.

The Rives-Stoppa procedure was performed on both sides of the abdominal wall in all specimens. The anterior and posterior component separation procedures were performed on one side in each specimen, such that each specimen functioned as its own control. The side and procedure to start with were randomly assigned. Before the surgical procedure, the abdominal dimensions were measured (*ie*, circumference at the umbilical level, distance from the xyphoid process to the pubic bone, and the distance from the anterior superior iliac spine [ASIS] to the ASIS).

Rives-Stoppa procedure

A median skin incision from the xiphoid process to the pubic bone was performed. Subsequently, subcutaneous tissue was dissected and the *linea alba* was identified. The *linea alba* was then incised longitudinally from the xyphoid process to the pubic bone. If necessary, adhesiolysis was performed. The rectus sheath was opened across its medial edge from the xyphoid process to the pubic bone. Thereafter, the rectus muscle was separated from the

posterior rectus sheath until the semilunar line was identified, concluding the Rives-Stoppa procedure. After this, either an anterior component separation or posterior component separation procedure was performed.

Anterior component separation procedure

After the Rives-Stoppa dissection, the subcutaneous tissue was dissected laterally from the anterior rectus sheath until the aponeurosis of the external oblique muscle was identified. Subsequently, the aponeurosis between the rectus sheath and the external oblique muscle was incised up to the external fascia of the internal oblique muscle, leaving the internal oblique muscle intact. Thereafter, the internal and external oblique muscles were separated laterally by blunt dissection, allowing for additional medialization of the anterior and posterior rectus sheath (Figure 1)

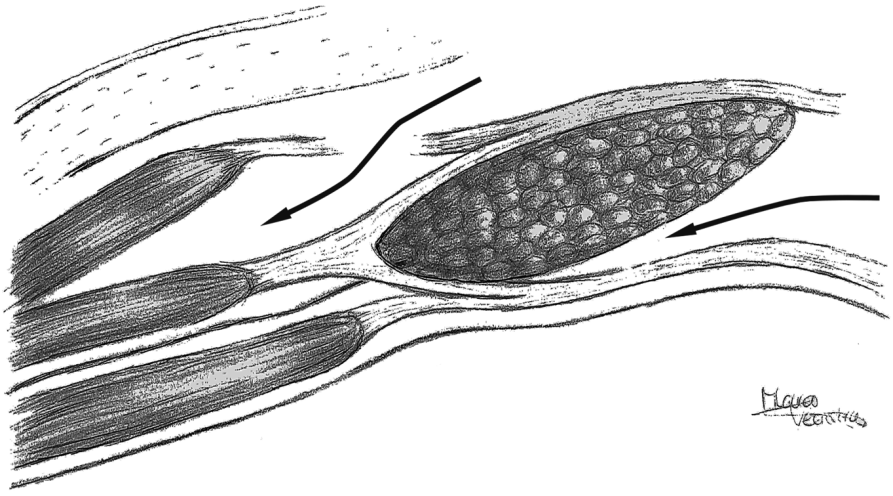

Figure 1. *Anterior component separation technique.* The external oblique muscle was incised up to the external fascia of the internal oblique muscle, leaving the internal oblique muscle intact. Blunt dissection was performed for medialization of the anterior and posterior rectus sheath.

Posterior component separation procedure

After the Rives-Stoppa dissection, the neurovascular bundles were identified. Subsequently, the lamina posterior of the internal oblique muscle and the transverse abdominis muscle were transected until either the fascia transversalis or the peritoneum, depending on the level of the abdomen, was identified. Thereafter, the transversal fascia or peritoneum was separated from the transverse abdominis muscle laterally by blunt dissection, allowing for additional medialization of the anterior and posterior rectus sheath (Figure 2). Any incidental defects created in the transversal fascia or peritoneum were closed with 4-0 sutures.

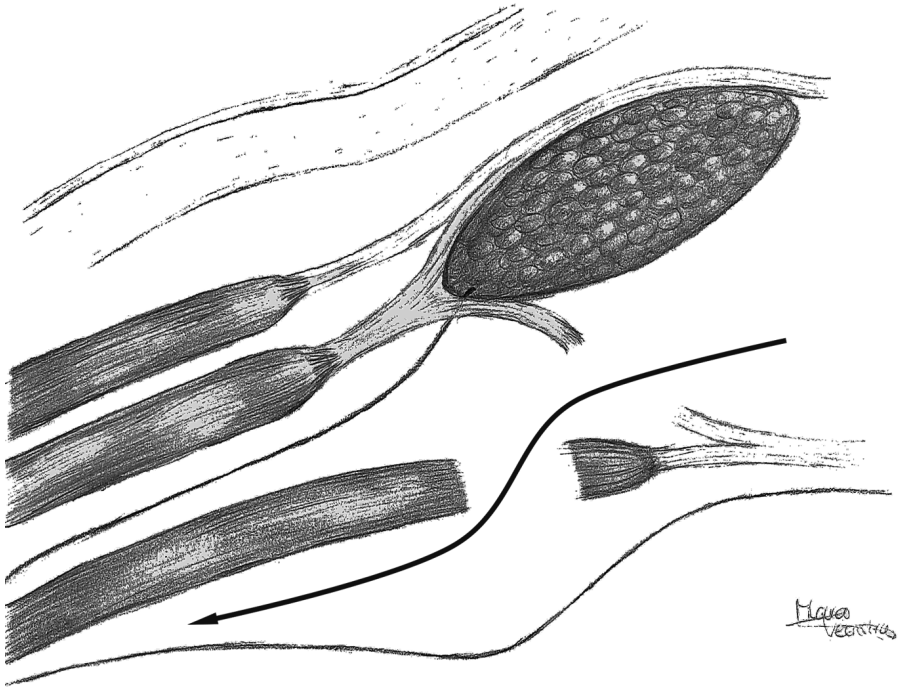

Figure 2. *Posterior component separation technique.* The lamina posterior of the internal oblique muscle and the transverse abdominis muscle were transected until the fascia transversalis or the peritoneum. Blunt dissection was performed for medialization of the anterior and posterior rectus sheath.

Measurements

A specially designed test setup was constructed to measure abdominal wall medialization in a standardized and reproducible fashion (Figure 3). Three identical Kocher clamps were placed along the anterior and posterior rectus sheath at three marked levels of the abdomen: (1) halfway between the xiphoid process and the umbilicus (upper abdomen); (2) At the umbilicus (mid abdomen); (3) Halfway between the umbilicus and the pubic bone (lower abdomen).

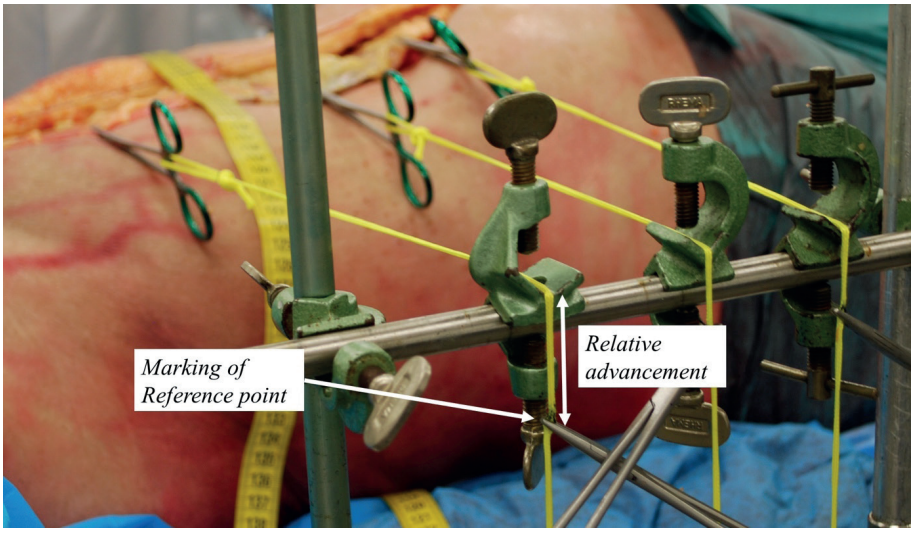

Figure 3. *Test setup*

Each clamp was attached to a 1-kg and subsequently 2-kg weight through a pulley system to ensure a force perpendicular to the linea alba. After opening the linea alba, the clamps were attached first, and the initial advancement was marked with a reference point on the wire (Figure 3). Subsequent medialization measurements were added up to this reference point (additional medialization). Therefore, these measurements are relative to the initial advancement after opening the linea alba. Measurements with three 1-kg weights (total 3 kg) and three 2-kg weights (total 6 kg) were performed separately. The measurements with the 2-kg weights were performed to assess whether medialization would increase when more lateral force was applied. All measurements were

performed with the use of an analogue-measuring gauge. After the three procedural steps, the following measurements were performed:

- Incision of the linea alba
    - Reference measurement
- Rives-Stoppa procedure
    - Advancement anterior rectus sheath
    - Advancement posterior rectus sheath
- Component separation procedures
    - Advancement anterior rectus sheath
    - Advancement posterior rectus sheath

Supplementary, total medialization measurements were taken only for the final 7 specimens included (7/13 specimens included for Rives-Stoppa and 6/10 specimens included for component separation). A string was fitted from the xiphoid process to the pubic bone to assess total medialization. During the reference measurement, the distance between the string and the edge of the incision through the linea alba was measured at the same 3 aforementioned abdominal levels while applying lateral force with three 1-kg or 2-kg weights.

Reporting of data and statistical analysis

Statistical analyses were performed using the SPSS Software Package (IBM SPSS Statistics for Windows, v 21.0, Armonk, NY). A sample-size calculation was not performed because comparative studies were unavailable. Therefore, no adequate effect estimation could be made. Discrete variables are presented as absolute numbers; continuous variables are presented as median and corresponding interquartile range (IQR) or graphically as mean and standard deviation (SD). Approximated overall medialization was calculated for each specimen as the mean of the medialization measured at the three abdominal levels. Medialization achieved in addition to the initial medialization after opening the linea alba is presented for measurements with three 1-kg weights. Only these relative measurements, representing net tension-free advancement after Rives-Stoppa and component separation, were used for the comparative analysis. Because of the relatively small sample size and non-normally distributed data, the nonparametric Wilcoxon signed-rank test was used.

Results

A total of 13 postmortem human specimens (5 females, 8 males) were included. The Rives-Stoppa procedure was performed on all 13 specimens, and the component separation procedure was performed on 10 specimens. One specimen was excluded from the component separation analysis because of an unnoticed Spigelian hernia, another specimen was excluded because of a large defect in the fascia transversalis (compromising the measurements), and another specimen was excluded because of a measurement error during the component separation procedure. Abdominal dimensions for each specimen are presented in supplement.

Additional medialization achieved after the Rives-Stoppa procedure alone

Additional medialization achieved after Rives-Stoppa alone is graphically presented (Figure 4). Additional medialization for the individual cases is presented in supplement. For the anterior rectus sheath, overall additional median medialization obtained was 1.2 cm (IQR: 0.3–2.2). Additional median medialization was 0.9 cm (IQR: 0–1.9) in the upper abdomen, 1.3 cm (IQR: 0.5–2.5) at the umbilicus, and 1.2 cm (IQR: 0.5–2.6) in the lower abdomen. For the posterior rectus sheath, overall additional median medialization obtained was 2.2 cm (IQR: 1.6–3.0). Additional median medialization was 1.9 cm (IQR: 1.3–3.1) in the upper abdomen, 2.0 cm (IQR: 1.5–3.3) at the umbilicus, and 2.4 cm (1.5–3.4) in the lower abdomen.

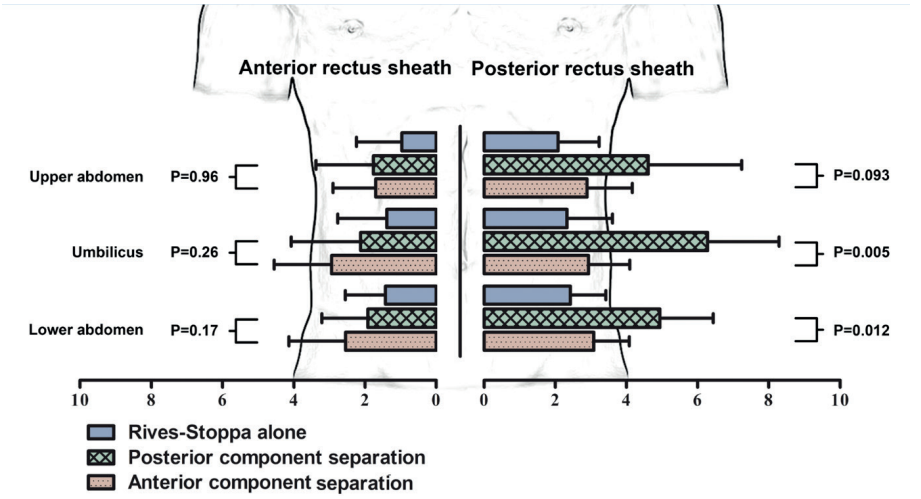

Figure 4. *Additional medialization after Rives-Stoppa and component separation techniques.* Medialization additional to initial medialization after opening the *linea alba* (in centimeters), columns represent mean medialization and error bars represent the standard deviation.

Additional medialization of the anterior rectus sheath after component separation

Additional medialization after the component separation procedures is graphically presented (Figure 4). Additional medialization for individual cases is presented in supplement. Overall additional median medialization obtained was 2.6 cm (IQR: 1.2–3.6) after anterior component separation and 1.9 cm (IQR: 0.4–3.4) after posterior component separation (P = .125). No statistically significant difference was present between additional medialization after anterior and posterior component separation at any abdominal level (Table 1). When subtracting additional medialization obtained by the Rives-Stoppa procedure alone, median extra medialization was 1.0 cm (IQR: 0.7–1.8) after anterior component separation and 0.5 cm (IQR: 0.1–1.2) after posterior component separation (P = .84).

Anterior rectus sheath							
	Additional medialization; median (IQR)				Total medialization; median (IQR)		
Position	**ACST**	**PCST**	**P**	**N**	**ACST**	**PCST**	**N**
Overall	2.6 (1.2-3.6)	1.9 (0.4-3.4)	0.125	10	-	-	-
Upper	1.5 (0.9-2.7)	2.1 (0.1-3.1)	0.96	10	5.0 (3.5-6.1)	5.0 (2.0 -6.1)	6
Umbilicus	2.7 (1.8-4.1)	1.7 (0.8-4.1)	0.26	10	6.5 (5.2-7.6)	5.7 (2.3-7.3)	6
Lower	2.8 (1.3-3.6)	2.5 (0.2-2.9)	0.17	10	6.1 (4.8-7.0)	5.0 (3.7-5.9)	6
Posterior rectus sheath							
	Additional medialization; median (IQR)				Total medialization; median (IQR)		
Position	**ACST**	**PCST**	**P**	**N**	**ACST**	**PCST**	**N**
Overall	3.0 (2.2-4.2)	5.2 (4.2-5.9)	**<0.001**	10	-	-	-
Upper	2.5 (2.1-4.4)	4.4 (3.3-5.3)	0.093	10	5.5 (4.1-7.1)	6.9 (4.9-9.4)	6
Umbilicus	3.0 (1.8-3.7)	6.0 (5.5-6.5)	**0.005**	10	5.8 (4.6-7.8)	9.4 (6.9-11.1)	6
Lower	3.1 (2.3-3.6)	4.6 (4.0-5.8)	**0.012**	10	5.8 (5.4-6.7)	7.4 (5.9-9.3)	6

Table 1. Medialization after anterior and posterior component separation

Legend: all measurements are presented in cm; CST: component separation; IQR inter quartile range.

Additional medialization of the posterior rectus sheath after component separation

Additional medialization after component separation procedures is graphically presented (Figure 4). Additional medialization for individual cases is presented in supplement. Overall additional median medialization obtained was 3.0 cm (IQR: 2.2–4.2) after anterior component separation and 5.2 cm (IQR: 4.2–5.9) after posterior component separation ($P < .001$). Statistically significant differences in medialization between the two techniques were present at the umbilicus and lower abdomen (Table 1). When subtracting the additional medialization obtained by the Rives-Stoppa procedure alone, median extra medialization was 0.8 cm (IQR: 0.1–1.3) after anterior component separation and 2.2 cm (IQR: 0.8–3.3) after posterior component separation ($P = .005$).

Total medialization

Total medialization was assessed in seven specimens for the Rives-Stoppa procedure and in six specimens for the component separation procedures. After incising the *linea alba* (reference measurement), overall median medialization with three 1-kg weights (total 3 kg) was 2.5 cm (IQR: 1.8–3.0). When applying double the weight to the linea alba (three 2 kg weights, total 6 kg), medialization increased by another 2.2 cm (IQR: 1.5–2.0). After the Rives-Stoppa procedure alone, total median medialization was 3.9 cm (IQR: 3.3–5.2) for the anterior and 4.5 cm (IQR: 3.6–6.5) for the posterior rectus sheath. Total medialization after the component separation procedures is summarized in the Table 1 and in Figure 5. Increased lateral force resulted in increased total medialization. However, additional medialization did not increase by applying increased force. For example, when attaching three 2-kg weights, overall additional medialization of the posterior rectus sheath remained similar (2.1 cm, after anterior component separation and 4.5 cm after posterior component separation).

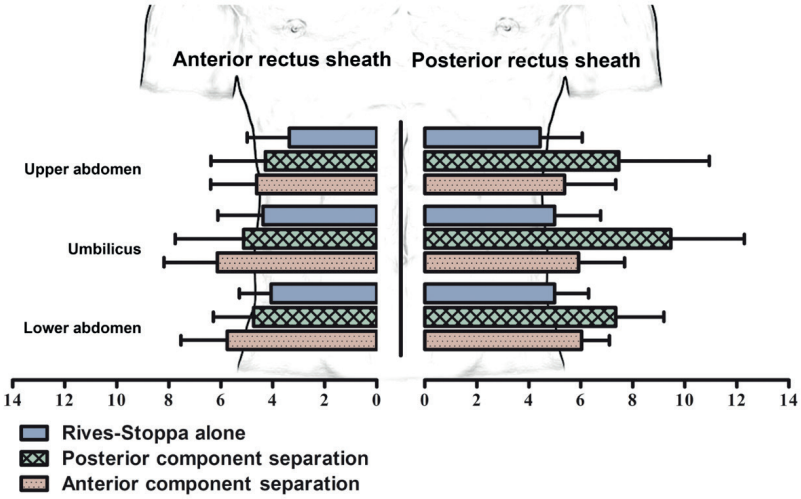

Figure 5. *Total medialization after Rives-Stoppa and component separation techniques.* Total medialization (in centimeters), columns represent mean medialization, and error bars represent the standard deviation.

Discussion

In this anatomic study on 13 postmortem human specimens, medialization, in addition to the initial medialization after opening the *linea alba*, was measured. The posterior component separation resulted in substantially more lateral advancement of the posterior rectus sheath as compared with the anterior component separation (3.0 cm versus 5.2 cm, $P < .001$). Medialization of the anterior rectus sheath was not significantly different between both techniques (2.6 cm versus 1.9 cm, $P = .125$). However, when considering the additional advancement to Rives-Stoppa alone, the anterior component separation may provide marginally more advancement of the anterior rectus sheath compared with the posterior component separation (1.0 cm vs 0.5 cm; $P = .84$). Medialization was usually lowest in the epigastric area of the abdomen. Applying more lateral force to the anterior and posterior rectus sheath (ie, pulling with more force on the rectus sheaths) did not result in an increased net effect of the Rives-Stoppa or component separation procedures. However, total medialization did increase when applying more lateral force. This implies that increased medialization, which can be observed when applying increased lateral force, may be obtained through stretching of the fascial layers.

Two previous anatomic studies evaluated the medial advancement after anterior component separation [19, 22]. However, both studies used a substantially different methodologic approach compared with this report and only reported total medialization after component separation. Total medialization measurements will likely be influenced more by individual patient variation [23]. Moreover, one of these studies used explanted abdominal walls, and therefore the studied situation deviated substantially from the in vivo condition. Nevertheless, the total medialization reported in the study by van Geffen *et al*. [22] (2.7–4.5 cm) is reasonably similar to the total medialization found in the present study. The study by Ramirez *et al.* [19] reported a generally higher total medialization of 5 cm in the epigastric region, 10 cm at the waistline, and 3 cm in the suprapubic region. Both our study and van Geffen *et al* .[22] found medialization to be lowest in the epigastric region and relatively similar in the umbilical region and lower abdomen. However, the halfway point between the *umbilicus* and the pubic bone might be too high to find a lower lateral advancement that is likely present in the adjacent suprapubic region [19]. A recently published study by Majumder *et al.* [24] reported an

overall mean total advancement after posterior component separation of 7.9 cm for the anterior and 9.6 cm for the posterior rectus sheath. In our series, we were unable to attain a similarly high total medial advancement for the anterior rectus sheath (median: 5.8 cm). However, in Majumder *et al.* [24], the initial total advancement after opening the linea alba and after the Rives-Stoppa procedure was also approximately 2 to 3 cm in comparison to our series. Therefore, the difference in results may be partially attributable to individual variation in the study samples or differences in the measurement methodology. Considering current and previous results, most advancement of the anterior rectus sheath is already obtained after retrorectus dissection alone [24]. For the posterior component separation in particular, every subsequent procedural step may provide some additional medialization. Dissection of the transverse abdominis muscle probably allows for less lateral strain on the integral rectus sheath, including anterior and posterior layers, providing additional medialization of the anterior rectus sheath [24].

Considering the limited sample size, exact effects of varying abdominal dimensions on medialization after component separation techniques are difficult to quantify. However, it is conceivable that obtained medialization, in absolute terms, will usually be greater as abdominal dimensions increase (supplement). Considering total medialization reported in present and other studies, fascial closure relatively free of tension may in general be achieved by Rives-Stoppa alone in IHs up to approximately 8 cm in width. In giant IHs, defined as 10 cm or more in width, component separation techniques will likely contribute substantially to tension-free fascial closure [7, 19, 22].

To date, two meta-analyses and one comparative observational study comparing clinical results after anterior and posterior component separation have been performed [20, 25, 26]. Both reports largely included single-armed retrospective studies, compromising direct comparison between both techniques. Nevertheless, neither of these reviews reported increased rates of surgical site infections, complications, reoperations, or recurrences after posterior component separation, reassuring the safety of this still relatively new technique [17, 26]. Moreover, Cornet *et al.* [17] reported a slightly decreased recurrence rate after posterior component separation. However, this could very well be attributable to differences in patient characteristics, given the observational design of the available evidence. Considering the present study

data, posterior component separation results in comparable medialization to anterior component separation and allows for the closure of large IHs. The advancement of the anterior rectus sheath was marginally higher after anterior component separation compared with posterior component separation. However, the anterior rectus sheath may withstand up to two times more lateral force as compared with the posterior rectus sheath [21, 27]. Therefore, this minor additional fascial strain might be of less concern. Meanwhile, posterior component separation likely allows for nearly tension-free fascial closure of the posterior rectus sheath in most cases, also preventing contact between abdominal contents and the mesh. Apart from component separation alone, recent observational studies have reported positive results of botulin toxin injections and preoperative progressive pneumoperitoneum [28, 29]. These techniques may allow for additional medialization and may diminish potentially negative effects of muscle contraction in the postoperative period. However, long-term reports on these techniques, to date, are scarce, and botulin toxin injections could in theory further weaken the abdominal musculature, which might impair long-term outcomes.

Recent meta-analyses did not report substantial differences in clinical outcomes between anterior and posterior component separation procedures [17, 25]. Theoretically, posterior component separation has several advantages. After transverse abdominis release, blunt dissection may be performed down to the psoas muscle. This allows for the placement of a mesh with a wider overlap compared with the retrorectus placement [18]. In addition, there is little room for mesh migration because of the large defect overlap. Therefore, less or even no fixation tags or sutures are required [26, 30]. Blood supply of the abdominal cutis, subcutis, and rectus muscles is provided by perforators of deep epigastric vessels and may be compromised by subcutaneous dissection, resulting in complications [31]. Anterior component separation has been associated with high rates of skin necrosis and wound infections [26, 32]. In addition, in spite of continuing wound drainage, subcutaneous dissection may lead to an increased risk of seromas [3].

Considering the present study data and recent systematic reviews, prospective clinical trials, although challenging, are needed to assess which component separation technique provides more favorable results in terms of short-term morbidity and long-term recurrence.

This study has several limitations. The specimens included did not suffer from any abdominal defect. Although this differs from the usual patient population treated by component separation techniques, it allowed for objective comparison of both sides of the abdomen. In addition, specimens with IHs would vary greatly, potentially compromising the analysis [10, 33]. Another limitation is the postmortem study design. Although fresh frozen specimens were used, tissue characteristics after death deviate from the in vivo situation. However, because within-specimen randomization and measurements relative to the initial advancement after opening the linea alba were performed, comparative analysis remains valid. Nevertheless, total medialization may be larger in an in vivo setting. In addition, muscle contraction during the postoperative period may negatively influence obtained medialization, causing additional fascial strain. Still, measurements in this study would be very difficult, if not impossible, to replicate in vivo. Finally, because of the small sample size, individual variation between the two abdominal sides might have contributed to the observed results. However, the side and procedure at which to begin were randomly assigned before opening the linea alba and therefore these effects will be mostly nondifferential.

In conclusion, based on the results obtained in 13 postmortem human specimens, IHs up to 8 cm in width may in general be closed by Rives-Stoppa alone. For IHs $\geq$ 10 cm in width, component separation techniques will be beneficial to attain tension-free fascial closure. Anterior component separation may provide marginally more medialization of the anterior rectus sheath as compared with posterior component separation. Posterior component separation yielded substantially more medial advancement of the posterior rectus sheath as compared with Rives-Stoppa and anterior component separation.

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Supplementary materials

Subject	Abdominal proportions		Additional medialization			Total mediazation
				Side 1	Side 2	Overall
1	Circumference Length ASIS-ASIS	65 27 23	Anterior rectus sheath Posterior rectus sheath	0.4 1.6	3.2 3.7	NA NA
2	Circumference Length ASIS-ASIS	78.5 27 22	Anterior rectus sheath Posterior rectus sheath	0.5 1.2	0.3 0.6	NA NA
3	Circumference Length ASIS-ASIS	79 28 23	Anterior rectus sheath Posterior rectus sheath	2.7 2.3	2.9 3.5	NA NA
4	Circumference Length ASIS-ASIS	94 30 30	Anterior rectus sheath Posterior rectus sheath	1.6 1.8	1.0 2.1	NA NA
5	Circumference Length ASIS-ASIS	97.5 39 30	Anterior rectus sheath Posterior rectus sheath	-0.1 2.4	-0.4 2.2	NA NA
6	Circumference Length ASIS-ASIS	98 34 28	Anterior rectus sheath Posterior rectus sheath	0.1 1.8	0.3 1.2	NA NA
7	Circumference Length ASIS-ASIS	66 29 24	Anterior rectus sheath Posterior rectus sheath	0.2 1.5	-0.6 1.4	1.4 3.1
8	Circumference Length ASIS-ASIS	68.5 31 22	Anterior rectus sheath Posterior rectus sheath	0.7 3.2	1.4 1.2	3.4 4.5
9	Circumference Length ASIS-ASIS	100 36 28	Anterior rectus sheath Posterior rectus sheath	1.1 1.8	1.3 2.1	3.4 4.1
10	Circumference Length ASIS-ASIS	83 30 22	Anterior rectus sheath Posterior rectus sheath	3.1 2.6	2.3 2.2	4.6 4.3
11	Circumference Length ASIS-ASIS	99 33 36	Anterior rectus sheath Posterior rectus sheath	1.0 NA	2.1 4.1	4.6 5.1
12	Circumference Length ASIS-ASIS	101 42 35	Anterior rectus sheath Posterior rectus sheath	1.6 2.8	2.5 2.8	5.7 6.5
13	Circumference Length ASIS-ASIS	97.5 34 27	Anterior rectus sheath Posterior rectus sheath	1.8 1.9	3.2 3.8	4.5 6.2

Appendix 1. Abdominal proportions and medialization after the Rives-Stoppa procedure

Legend: All measurements are presented in cm for one abdominal side. Overall medialization is presented for measurements with three 1 kg weights. The anterior and posterior component separation were performed on respectively side one and two. Abdominal length is the distance from the xiphoid process to the pubic bone. ASIS: anterior superior iliac spine; NA: not available.

Subject	Abdominal proportions			Additional medialization		Total medialization	
				Anterior CST	Posterior CST	Anterior CST	Posterior CST
1	Circumference	65	Anterior rectus sheath	1.2	4.0	NA	NA
	Length	27					
	ASIS-ASIS	23	Posterior rectus sheath	2.4	5.5	NA	NA
2	Circumference	78.5	Anterior rectus sheath	1.1	0.4	NA	NA
	Length	27					
	ASIS-ASIS	22	Posterior rectus sheath	1.3	3.0	NA	NA
3	Circumference	79	Anterior rectus sheath	NA	NA	NA	NA
	Length	28					
	ASIS-ASIS	23	Posterior rectus sheath	NA	NA	NA	NA
4	Circumference	94	Anterior rectus sheath	2.7	1.6	NA	NA
	Length	30					
	ASIS-ASIS	30	Posterior rectus sheath	2.9	5.8	NA	NA
5	Circumference	97.5	Anterior rectus sheath	1.7	-0.4	NA	NA
	Length	39					
	ASIS-ASIS	30	Posterior rectus sheath	4.2	4.3	NA	NA
6	Circumference	98	Anterior rectus sheath	NA	NA	NA	NA
	Length	34					
	ASIS-ASIS	28	Posterior rectus sheath	NA	NA	NA	NA
7	Circumference	66	Anterior rectus sheath	0.2	-0.4	2.0	1.9
	Length	29					
	ASIS-ASIS	24	Posterior rectus sheath	1.7	3.8	3.1	5.2
8	Circumference	68.5	Anterior rectus sheath	NA	NA	NA	NA
	Length	31					
	ASIS-ASIS	22	Posterior rectus sheath	NA	NA	NA	NA
9	Circumference	100	Anterior rectus sheath	4.2	1.6	6.4	3.6
	Length	36					
	ASIS-ASIS	28	Posterior rectus sheath	3.0	6.1	5.1	8.1
10	Circumference	83	Anterior rectus sheath	4.0	2.3	6.3	3.7
	Length	30					
	ASIS-ASIS	22	Posterior rectus sheath	3.2	5.1	4.7	6.5
11	Circumference	99	Anterior rectus sheath	2.8	3.6	6.0	6.6
	Length	33					
	ASIS-ASIS	36	Posterior rectus sheath	2.6	9.4	5.6	12.3
12	Circumference	101	Anterior rectus sheath	2.6	2.7	6.2	6.4
	Length	42					
	ASIS-ASIS	35	Posterior rectus sheath	4.3	4.6	8.0	8.3
13	Circumference	97.5	Anterior rectus sheath	3.5	3.3	6.1	6.1
	Length	34					
	ASIS-ASIS	27	Posterior rectus sheath	4.3	5.3	6.8	8.1

Appendix 2. Abdominal proportions and medialization after the component separation procedure

Legend: All measurements are presented in cm for one abdominal side. Overall medialization is presented for measurements with three 1 kg weights. Abdominal length is the distance from the xiphoid process to the pubic bone. ASIS: anterior superior iliac spine; NA: not available; CST: component separation.

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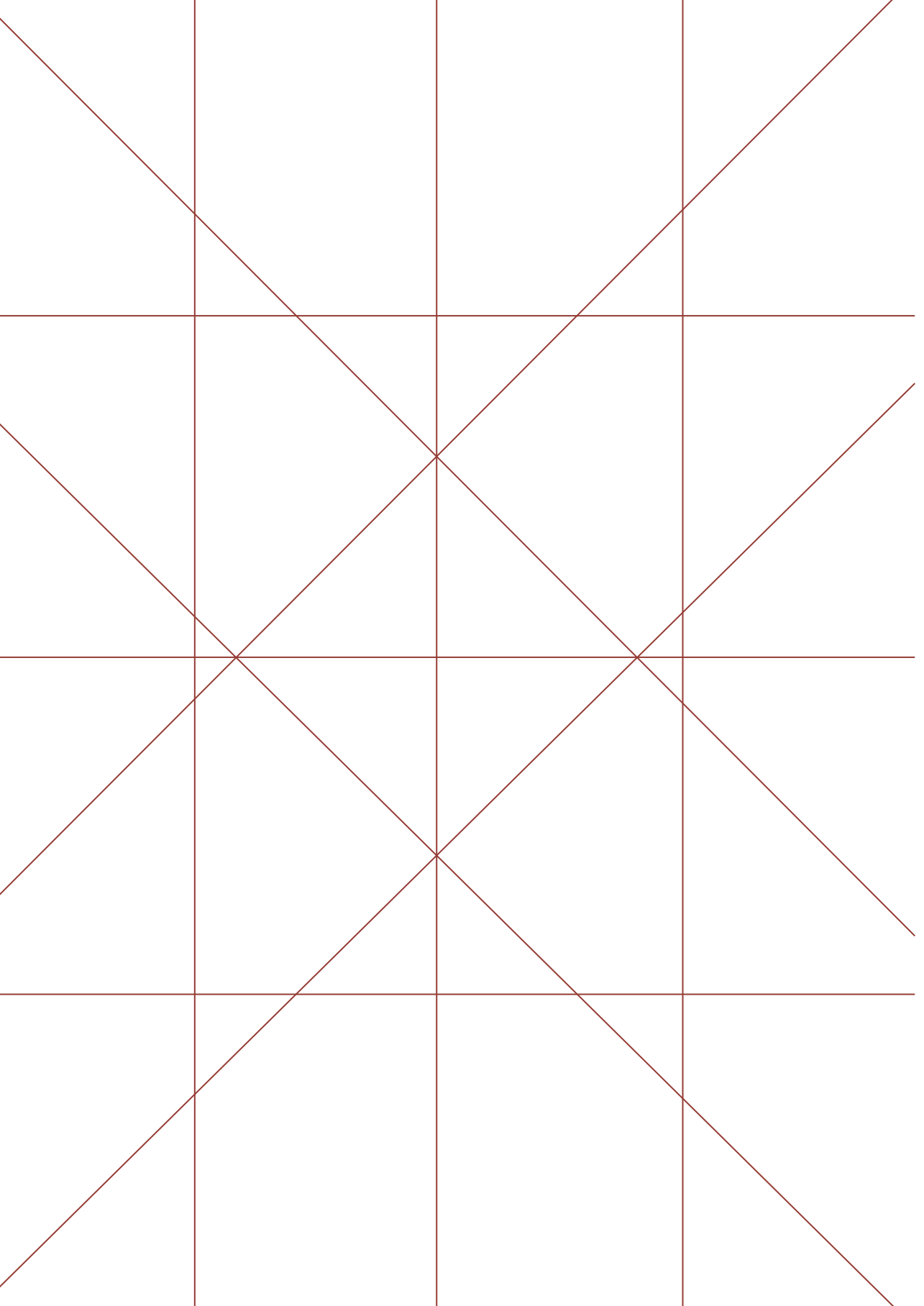

Chapter 5

Zinc-impregnated mesh for abdominal wall repair reduces infection in a rat model of peritonitis

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Abstract

Background

The objective of this study was to assess whether a zinc-impregnated polypropylene mesh (ZnMesh) has better antibacterial properties in a contaminated environment compared with a regular polypropylene mesh.

Materials and methods

Thirty-eight Wistar Han rats underwent cecal ligation and puncture to induce peritonitis 24 h before implantation of an intraperitoneal ZnMesh or a regular polypropylene mesh. Primary outcome was the number of colony forming units (CFU) per sample (mesh and abdominal wall). Secondary outcomes were macroscopic (incorporation of mesh, abscesses, and adhesions on mesh surface) and histological (inflammatory cell reaction, mesh-specific parameters, and collagen deposition) parameters. All outcomes were evaluated after 30 and 90 d.

Results

After 30 d, no significant difference in CFU per sample was present between the ZnMesh and control groups. After 90 d, a lower number of CFU per sample was present in the ZnMesh group compared with the control group (trypticase soy agar with 5% sheep blood: 0 $\log_{10}$ CFU/sample IQR: 0-1.40 *versus* 1.58 $\log_{10}$ CFU/sample IQR: 0-4.30, $P = 0.012$; MacConkey: 0 $\log_{10}$ CFU/sample IQR: 0-2.65 *versus* 1.18 $\log_{10}$ CFU/sample IQR: 0-4.04, $P = 0.438$). After 90 d, the percentage of adhesions on mesh surface was significantly higher in the ZnMesh group (95% IQR: 60%-100% *versus* 50% IQR: 23%-75%, $P = 0.029$). No differences were seen in other macroscopic outcomes or histology.

Conclusions

A significantly lower number of CFU per sample was found in the ZnMesh group after 90 d. After 30 d, no statistically significant differences in CFU per sample were seen. This result suggests that the ZnMesh group has better antibacterial properties in a contaminated environment. However, this is at the cost of a significantly higher percentage of adhesions.

Introduction

Prosthetic implants are used for the repair of abdominal wall hernias, and their application results in significantly lower recurrence rates (1). However, the use of a nonabsorbable synthetic mesh for hernia repair in a contaminated field remains controversial given the higher risk of postoperative infection (2). Mesh infection is one of the most severe and disastrous complications after hernia repair and may require surgical removal of the implanted scaffold (3). Mesh explantation may lead to patient morbidity, prolonged hospital admission, and increasing healthcare costs (4). Biologic implants have been promoted for contaminated fields for a long time without presenting high-level evidence (5). In a study performed by Rosen *et al.*, the overall hernia recurrence was 31% using a biological mesh in a contaminated abdominal wall defect, after a follow-up of 21.7 mo (range 1-74 mo) (6). In addition, higher cost of biologic meshes compared with synthetic meshes is a drawback (7). Despite the wide selection of available meshes, the search for the ideal mesh to use in contaminated fields is still ongoing. To reduce the incidence of infection, several antibacterial mesh coatings have previously been investigated (8, 9). Bacterial attachment and proliferation are necessary steps in the development of an infection depending on several factors, such as the type of polymer and its structure (10). Recently, it was found that zinc ions are able to inhibit multiple activities of bacteria, for instance transmembrane proton translocation, glycolysis, and acid tolerance (11). In addition, zinc oxide may disturb metabolic pathways and exhibit an antibacterial effect on both *Escherichia coli* and *Staphylococcus aureus* (11). Until now, the polypropylene mesh incorporated with zinc ions (ZnMesh) has only been examined in *in vitro* models.

The primary objective of this animal study was to determine whether a polypropylene mesh incorporated with zinc ions has better antibacterial properties when placed in a contaminated environment compared with a regular polypropylene mesh. The secondary objectives were to assess ingrowth of the mesh, abscess formation, and adhesion. Furthermore, histological parameters were assessed, such as inflammatory cell response, mesh-specific parameters, and collagen deposition.

Material and methods

The study protocol was approved by the Ethical Committee on Animal Experimentation of the Erasmus University Medical Center (Rotterdam, the Netherlands, license number: AVD101002015179) and was performed in accordance with the ARRIVE guidelines on the use of laboratory animals (12).

Animals

Thirty-eight male Wister Han rats, weighing 280-325 g, were purchased from Charles River Laboratories (‘s-Hertogenbosch, the Netherlands). The animals were bred under specific pathogen-free conditions. All rats were housed in pairs in individually ventilated cages under 12 h dark/light cycles. The temperature was kept between 20°C and 24°C, and relative humidity was 50% to 60% in the laboratory. Standard rat chow and water was provided *ad libitum*. The rats were accustomed to laboratory conditions 1 wk before the start of the experiment.

Meshes

Regular polypropylene meshes and ZnMesh were provided by the producer (Parx Plastics, Rotterdam, the Netherlands). An existing polypropylene mesh was chemically and physically treated with dietary zinc (Zn 2+). This treatment resulted in positive ionic surface of the polymer. Zinc ions do not migrate during time, and the ZnMesh remains biologically inert. It was hypothesized that the positive ionic surface makes the surface hostile to bacteria, reduces the capability to form biofilm, and interferes with the bacteria proliferation without releasing ions.

Surgical procedure

Preoperatively, 38 rats were randomly divided into two groups to receive either the ZnMesh (n = 20) or regular polypropylene mesh (n = 18). These two groups were again randomly divided into two groups for a follow-up of 30 or 90 d. Experiments were done under aseptic conditions in an operation room for small animals. All rats were anesthetized with a combination of isoflurane and oxygen inhalation. Preoperatively, a single dose of 0.05 mg/

kg buprenorphine was administered subcutaneously. After anesthesia, the abdominal skin was shaved, disinfected with alcohol 70%, and subsequently a 3-cm midline incision was performed, to enter the abdominal cavity.

Cecal Ligation Puncture Model

The cecal ligation puncture model was used for the induction of peritonitis (13). On day 0, ligation of the cecum was performed just distal to the ileocecal valve with a nonabsorbable polyamide suture (5-0 Ethilon; Ethicon, Inc., Sommerville, NJ), without interrupting the bowel continuity. Subsequently, a puncture with an 18-gauge needle was performed distally in the cecum. The fascia and skin were closed in two layers with running absorbable polyglycolic acid sutures (5-0 Safil; B. Braun, Melsungen, Germany). Postoperatively, all animals received 5 mL sodium chloride 0.9 per cent subcutaneously and were placed under a heating lamp to prevent hypothermia. After 24 h (day 1), all rats were anesthetized with the same inhalation mixture as on day 0 and the abdominal cavity was disinfected and reopened. The necrotic or ischemic section of the cecum was resected and the abdominal cavity was rinsed with warmed phosphate buffer at 37°C. Aminoglycoside antibiotics (gentamicin) were administered with a dosage of 6 mg per kilogram intramuscularly. A sterile mesh of 2.5 × 3 cm (7.5 cm^2) was placed intraperitoneally and was fixated with six transmuscular nonabsorbable sutures (5-0 Ethilon, Ethicon, Inc). Again, the fascia and skin were closed in two layers with a running absorbable suture (5-0 Safil; B. Braun). Subsequently, the rats received 5 mL sodium chloride 0.9 per cent and were placed under a heating lamp to prevent hypothermia immediately after surgery.

Survival and wellness

All rats were weighed daily during the first 4 d postoperatively. Animals were inspected for signs of pain or surgical site occurrences. In addition, all animals were checked daily by an animal care taker. A 12-point wellness and behavior scoring system was used to assess wellness and behavior (Supplementary materials, Table 1) (14). Rats were removed from the experiment when they reached the humane endpoint (a wellness score of <5 points or weight loss of more than 20%).

Sacrifice

After 30 and 90 d, euthanasia was performed under anesthesia (combination of isoflurane and oxygen inhalation) by subsequent cardiac cut (15).

Microbiology

The abdominal skin was shaved and disinfected with alcohol 70%. The ventral abdominal wall was opened via a U-shaped incision, and a picture of the mesh was taken (figure 1). Full-thickness abdominal wall samples including mesh were sampled aseptically. The samples measured 1.0 × 1.0 cm and were stored on ice in a tube with 2 mL sterile phosphate buffered saline. Subsequently, samples were homogenized for 30 s (IKA T25 ULTRA-TURRAX). Samples were plated in serial dilutions onto MacConkey Agar (Becton Dickinson, Etten-Leur, the Netherlands) to select for gram-negative bacteria. The samples were also plated on trypticase soy agar with 5% sheep blood (Becton Dickinson) to select for a wide variety of microorganisms. A maximum of three bacteria were identified using the matrix-assisted laser desorption or ionization time-of-flight analyzer (MALDI Biotyper; Bruker Daltonics, Bremen, Germany). The plates were incubated at 37°C for 24 h, and the amount of colony forming units (CFU) per full-thickness abdominal wall and mesh sample (CFU/sample) was counted. Second, a qualitative analysis was performed using 30 µL inoculation loop. For confirmation of the microbiological flora of healthy Wistar Han rats, additional analyses were performed. Feces from five different healthy Wistar Han rats from the same strain and area (Charles River Laboratories) were collected directly from the cecum and analyzed with the same methods as described previously.

Macroscopy

All parameters were determined by two blinded, independent observers. In case of disagreement, the results were discussed between the two blinded observers and consensus was reached.

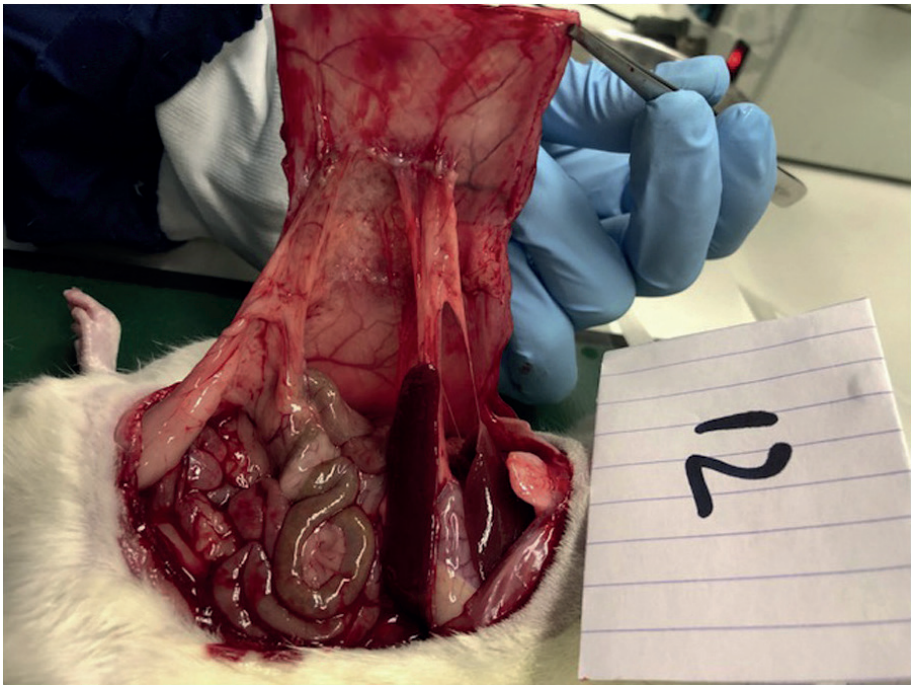

Figure 1. Photograph (color) taken during the macroscopic assessment. Photo taken during sacrifice showing the inner abdominal wall and a polypropylene mesh without zinc coating.

Ingrowth of the mesh

All edges of the mesh were lifted from the abdominal wall and inspected for ingrowth. Ingrowth was computed by using a caliper to examine adhering tissue between abdominal wall and mesh presented as a percentage (15-17).

Adhesions

Adhesions were determined in a qualitative manner by using the Zühlke score (Supplementary materials, Table 2) and in a quantitative manner by two independent observers until consensus was reached and expressed in percentages on the mesh surface (18).

Abscesses

The amount and size of abscesses at the abdominal wall and in the abdominal cavity were assessed visually by using a scoring system (Supplementary materials, Table 3) (19).

Histology

Full-thickness (mesh and abdominal wall muscle) samples of 1.0 × 0.5 cm were collected in-between sutures. All samples were fixated in 4% formalin for 24 h. Next, the fixated samples were embedded in paraffin. Sections of 4 μm were cut (Leica RM2255 microtome; Leica Biosystems, Wetzlar, Germany) and stained with Sirius Red (Ventana Benchmark Special Stains system; Hoffmann-La Roche, Bazel, Switzerland) or hematoxylin and eosin staining (Ventana Symphony automated staining instrument; Hoffman-La Roche, Bazel, Switserland). All histological evaluations were performed by a pathologist (MCvG) who was blinded for the type of mesh. The inflammatory cell reaction was evaluated by counting the amount of cells per high-power field (40× magnification), using a scoring system described by Peeters *et al*. (Supplementary materials, Table 4) (20). Mesh-specific parameters were evaluated using a modified scoring system assessing scaffold degradation, fibrous encapsulation, cellular infiltration, and neovascularization (Supplementary materials, Table 5) (20). Collagen deposition, as visualized by Sirius Red staining, around the mesh and abdominal wall were evaluated using a scoring system described by Deeken *et al*. (Supplementary materials, Table 6) (21).

Statistical analysis

A power calculation was not performed because no earlier comparison in the number of CFU between meshes was performed. Outcomes are presented as median (interquartile range). Survival, macroscopy, histology, and microbiological results were compared performing a χ^2 test and a nonparametric Mann-Whitney *U* test for independent samples. Reported *P*-values are two-sided, and P-values < 0.05 were considered statistically significant. IBM SPSS Statistics for Windows, version 24.0.0.1, Armonk, NY, was used.

Results

Survival

Initially, all rats survived the first operation. In the first 4 d postoperatively, 12 rats (32%) of the 38 rats died of sepsis. Nine of 12 rats belonged to the ZnMesh group, and three of 12 rats belonged to the control group. However, two of nine rats from the ZnMesh group had never received a ZnMesh as they died before the second surgery and subsequent mesh implantation. This difference in two groups was not significantly different ($P = 0.086$). One of 12 rats died at day 15 for an unknown reason. None of the rats reached the humane endpoint. Finally, 26 rats (68.5%) remained for follow-up with 12 rats (46.2%) in the 30-day follow-up group and 14 (53.8%) in the 90-day follow-up group (Table 1).

	Start N (%)	Death N (%)	Total FU N (%)	30 days FU N	90 days FU N
ZnMesh	20 (33)	9 (45)	11 (42)	6	5
Control	18 (47)	3 (17)	15 (58)	6	9
Total	38 (100)	12 (32)	26 (100)	12	14

Table 1. Distribution of survival and follow-up per group. FU = Follow-up

Cecal Ligation Puncture Model

Sixteen rats (42.1%) had a necrotic cecum and 15 rats (39.5%) had an ischemic cecum (Table 2). All animals showed symptoms of sepsis, including weight loss, abnormal posture, ocular exudates, apathetic behavior, diarrhea, shivering, and piloerection.

Cecum	N (%)
Necrotic	16 (42.1)
Ischemic	15 (39.5)
Ischemic and necrotic (combination)	1 (2.6)
No changes (normal cecum)	2 (5.3)
No second operation	2 (5.3)
Missing	2 (5.3)
Total	38 (100)

Table 2. Cecal Ligation Puncture Model – Cecum

Microbiology

At 30 d, no significant difference in CFU/sample was present between the ZnMesh and control groups (Table 3) At 90 d, a significantly lower number of CFU/sample were present in the ZnMesh group compared with the control group (0 $\log_{10}$ CFU/sample, IQR 0-1.40 *versus* 1.58 $\log_{10}$ CFU/sample IQR 0-4.30, P = 0.012, Table 3). Mainly, *Enterococcus* and *Staphylococcus*, both gram-positive bacteria, were identified. In an additional experiment, mostly *Escherichia* (a gram-negative bacterium) and *Lactobacillus* (a gram-positive bacterium) were identified in the feces of five Wistar Han rats. Furthermore, *Enterococcus* and *Staphylococcus* were identified.

30 days	ZnMesh (N = 6)	Control (N = 6)	p-value
MacConkey ($\log_{10}$ CFU/sample)	3.75 (1.11 - 4.72)	2.93 (1.11 - 5.85)	1.000
TSA-SB ($\log_{10}$ CFU/sample)	3.98 (1.94 – 6.08)	3.98 (1.94 – 6.08)	0.818

90 days	ZnMesh (N = 5)	Control (N = 9)	p-value
MacConkey ($\log_{10}$ CFU/sample)	0 (0 – 2.65)	1.18 (0 – 4.04)	0.438
TSA-SB ($\log_{10}$ CFU/sample)	0 (0 – 1.40)	1.58 (0 – 4.30)	**0.012**

Table 3. Microbiology, 30 and 90 days of follow-up. Statistically significant values ($P < 0.05$) are given in bold.

Macroscopy, ingrowth

There were no significant differences in ingrowth of the mesh in percentages in both groups at both time points (30 d of follow-up: 75 [IQR 65-88] percent *versus* 78 [IQR 70-81] percent, P = 1.000; 90 d of follow-up: 66 [IQR 49-74] percent *versus* 59 [IQR 47-75] percent, P = 0.797, see Table 4).

30 days	ZnMesh (N = 6)	Control (N = 6)	p-value
Ingrowth (%)	75 (65-88)	78 (70-81)	1.000
Adhesions (%)	85 (74-96)	75 (56-93)	0.394

90 days	ZnMesh (N = 5)	Control (N = 9)	p-value
Ingrowth (%)	66 (49-74)	59 (47-75)	0.797
Adhesions (%)	95 (60-100)	50 (23-75)	**0.029**

Table 4. Macroscopy: ingrowth and adhesions (%) 30 and 90 days of follow up. Median (interquartile range). Statistically significant values ($P < 0.05$) are given in bold.

Macroscopy, adhesions

The highest Zühlke score in the ZnMesh group was Zühlke 3 in six rats (100%) and Zühlke 3 in five rats (100%) after 30 and 90 d, respectively. In the control group, the Zühlke score was 3 in four rats (80%) after 30 d. After 90 d, eight rats (88.9%) had a Zühlke 3 score. The highest Zühlke score in the control group was Zühlke 4 in two rats (20%) after 30 d of follow-up and in one rat (11.1%) after 90 d of follow-up. No significant differences were found after 30 d of follow-up in adhesions expressed in percentage (85 [IQR 74-96] percent *versus* 75 [IQR 56-93] percent, $P = 0.394$, Table 4). The percentage of adhesions on the mesh surface was significantly higher in the ZnMesh group after 90 d (95 [IQR 60-100] *versus* 50 [IQR 23-75], $P = 0.029$, see Table 4).

Macroscopy, abscesses

Macroscopically, only one rat developed one small abscess located on the mesh. This rat had a regular polypropylene mesh and was randomized for the 90-day follow-up group.

Histology

Histological analyses showed no significant differences in inflammatory cell reaction (overall inflammatory cell reaction [P = 0.781], eosinophils-neutrophils [P = 0.274], macrophages-foreign body giant cells [P = 0.432], and mononuclear cells [P = 0.432], Table 5) and mesh-specific parameters (scaffold degradation [P = 0.820], fibrous encapsulation [P = 0.193], cellular infiltration [P = 0.595], neovascularization [P = 0.820], and extracellular matrix deposition [P = 0.820], Table 6). In addition, no significant differences were found in collagen deposition across the four groups (P = 0.257, Table 6). Four rats showed microscopically signs of abscess formation, at both time points with one rat implanted with a ZnMesh and one rat in the control group.

	ZnMesh (N = 6) 30 days	Control N = 6 30 days	ZnMesh N = 5 90 days	Control N = 9 90 days	P-value
Inflammatory cell reaction	3 (2-3)	3 (3-3)	3 (2-3)	3 (2-3)	0.781
Eosinophils-neutrophils	3 (1-3)	3 (3-3)	3 (0-3)	2 (0-3)	0.274
Macrophages-foreign body giant cells	3 (2-3)	3 (2-3)	3 (1-3)	3 (3-3)	0.432
Mononuclear cells	3 (2-3)	3 (2-3)	3 (1-3)	2 (1-3)	0.432

Table 5. Histology: inflammatory cell reaction. Median (interquartile range)

	ZnMesh N = 6 30 days	Control N = 6 30 days	ZnMesh N = 5 90 days	Control N = 9 90 days	P-value
Scaffold degradation	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0.820
Fibrous encapsulation	1.5 (1-2)	1 (1-1)	2 (1-2)	2 (1-2)	0.193
Cellular infiltration	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-1)	0.595
Neovascularization	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0.820
Extracellular matrix deposition	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0.820
Collagen deposition	3.5 (2.75-4)	2.5 (2-3)	3 (2-3.5)	3 (2-4)	0.257

Table 6. Histology: mesh specific parameters. Median (interquartile range)

Discussion

In this rat study, a polypropylene mesh impregnated with zinc ions was compared with a regular polypropylene mesh in a contaminated environment. After a follow-up of 90 d, a lower CFU per sample was found in favor of the ZnMesh on the trypticase soy agar with 5% sheep blood agar plate. This difference was not seen at the other agar plates after a follow-up of 30 d. In addition, a higher percentage adhesions on the mesh was found in the ZnMesh group after 90 d of follow-up. Adhesion formation is an important parameter for investigating the biocompatibility of meshes. Prolonged exposure to the mesh and/or the addition of zinc ions could result in more extensive reactions and could be an explanation for this finding. The exact reason for this difference in adhesions between groups remains unclear. No differences were found in macroscopically assessed ingrowth and abscesses between meshes. The histological parameters including inflammatory cell reaction, mesh-specific parameters, and collagen deposition were not significantly different between the two groups after 30 and 90 d. However, the power calculation was not based on these secondary outcomes and might therefore lack enough power to detect a difference.

The mortality after peritonitis induction was 32%, which is slightly higher when compared with previous literature using this cecal ligation puncture model (10%-28%) (13, 16, 17, 22, 23) A notable high mortality rate was seen in the ZnMesh group (nine ZnMesh animals *versus* three control animals). However, two of these nine rats never received a ZnMesh. These two rats died before implantation due to the implications of the sepsis based on the induced peritonitis. This difference in dead animals between the two groups and mesh types was not significantly different ($P = 0.086$). An explanation for this high mortality could be a less resistant strain of animals for infection or the presence of a more fulminant abdominal infection due to the experimental set-up.

Various meshes are available for the repair of an abdominal wall hernia in the presence of intra-abdominal infection. Still, the introduction of a mesh reduces the amount of bacteria needed to result in an infection by a factor 10^4 (24). The evidence for using biological mesh in contaminated abdominal

wall hernia repair is still limited (25). The aim of this experimental study was to add knowledge in this search for an ideal mesh to use in a contaminated environment for ventral hernia repair. The occurrence of a clinically relevant infection depends on both patient-related factors as well as the quantity of bacteria (26). An earlier conducted study by Tubre *et al*. showed that contamination with more than 10^5 CFU per gram may result in wound infections (26). Pathogens found in humans at surgical site infection were *S. aureus* and *Enterococcus* species (26). These organisms are the same as found in this study, which is performed in rats. Recently, a study showed that rats represent a good preclinical model in hernia and mesh research (27). In addition, future studies may consider electron microscopy for the evaluation of biofilm formation because this supports bacterial attachment to the mesh (26). The results of this present study may encourage us to conduct more research with zinc-impregnated meshes in a contaminated environment, to decrease the risk of surgical site infection or mesh infection after abdominal wall repair. However, a comparison should be made with different types of meshes because the placement of a polypropylene mesh intraperitoneally is certainly not the standard (28). New *in vitro* and *in vivo* studies could be performed with direct inoculation on the mesh surface with a known quantity and quality of the bacteria, and to compare this with different permanent synthetic, slowly resorbable synthetic and nonsynthetic (biological) meshes.

Limitations

Information regarding the regular microbiological flora was required to differentiate between contamination during surgery or an effect of the ZnMesh on a fewer amount of CFU per sample in favor of the ZnMesh. However, microbiological assessment of preoperative and intraoperative feces was lacking in this study. Nevertheless, Charles River laboratories kindly provided data regarding the microbiological flora of these rats. These data showed that they found comparable microbiological flora as was found in this present study. Besides, feces from rats from the same laboratory, strain and area were analyzed with the same methods as in this experiment to confirm the additional data from Charles River laboratories. With these supplementary tests, an effect of the ZnMesh on CFU per sample was confirmed. Consensus and comparability among animal experiments to study mesh behavior is lacking (29). Several differences between this experimental study and the

human situation were present. Examples are the treatment of abdominal sepsis and the relative dimensions of the mesh (15). ecause this experimental study was performed with animals, these results may not be translated to the human population directly.

Conclusion

A significantly lower number of CFU per sample were found in the ZnMesh group after 90 d. However, no differences in other outcomes were found between the ZnMesh and control groups after 30 d of follow-up. These results suggest that a zinc-impregnated mesh has antibacterial properties when placed in a contaminated environment, compared with a regular polypropylene mesh. However, this is at the cost of a significantly higher percentage of adhesions. In addition, an antiadhesive mesh coating could be added to reduce adhesions. Further experiments are required to confirm this hypothesis.

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Supplementary materials

Parameter	Grading	Score
Activity	Normal - medium - low	2 - 1 - 0
Fur	Smooth - fluffy - erect	2 - 1 - 0
Eyes	Clean and open - clean and closed - dirty and closed	2 - 1 - 0
Able to stand strait	Yes - no	1 - 0
Posture	Normal - modestly curled - fully curled up	2 - 1 - 0
Position on feet	Normal - high	1 - 0
Solitary	Yes - no	0 - 1
Shivering	Yes - no	0 - 1

Table 1. 12-point wellness and behaviour scoring system

Grade	Description
0	No adhesions
1	Minimal, filmy adhesions requiring little blunt dissection
2	Moderate adhesions requiring blunt and partly sharp dissection; beginning of vascularization
3	Strong adhesions; lysis possible by sharp dissection only, clear vascularization
4	Very strong adhesions; lysis possible by sharp dissection only; organs attached (damage to organs difficult to prevent)

Table 2. Adhesions: Zühlke score system

Score	Definition
0	No abscess present at the site
0.5	One small abscess present at the site
1	Several small abscesses present at the site
2	Medium abscess present at the site
3	Large or several medium abscesses present at the site
4	One very large or several large abscesses present at the site

Table 3. Abscess scoring system

	0	**1**	**2**	**3**
Inflammatory cell reaction	0 - 50	51 - 100	101 - 150	>150
Eosinophils-neutrophils	0	1 - 5	6 - 10	>10
Macrophages-foreign body giant cells	0	1 - 5	6 - 10	>10
Mononuclear cells	0 - 10	11 - 50	51 - 100	>100

Table 4. Inflammatory cell reaction. All parameters were scored as number of cells per high-power field at x40 magnification

	0	1	2
Scaffold degradation	Original scaffold intact, borders clearly demarcated	Scaffold partially degraded, layers separated by cells, blood vessels, host tissue, etc.	Scaffold completely degraded, no evidence of original scaffold
Fibrous encapsulation	Extensive encapsulation (50-100% of periphery)	Moderate encapsulation (>0-50% of periphery)	No fibrous encapsulation
Cellular infiltration	Cells in contact with scaffold, no infiltration	Cells infiltrate scaffold, but none reach center	Cells penetrate into center of scaffold
Neovascularization	No blood vessels present	Vessels infiltrate scaffold but none reach center of scaffold	Vessels penetrate into center of scaffold
Extracellular matrix (ECM) deposition	No host ECM deposition	Host ECM deposited inside scaffold, but not at center	Host ECM deposited inside scaffold, including center

Table 5. Mesh-specific parameters

Score	Definition
0	No response
1	Minimal/barely detectable
2	Mild/slightly detectable
3	Moderate/easily detectable
4	Marked very evident

Table 6. Collagen deposition

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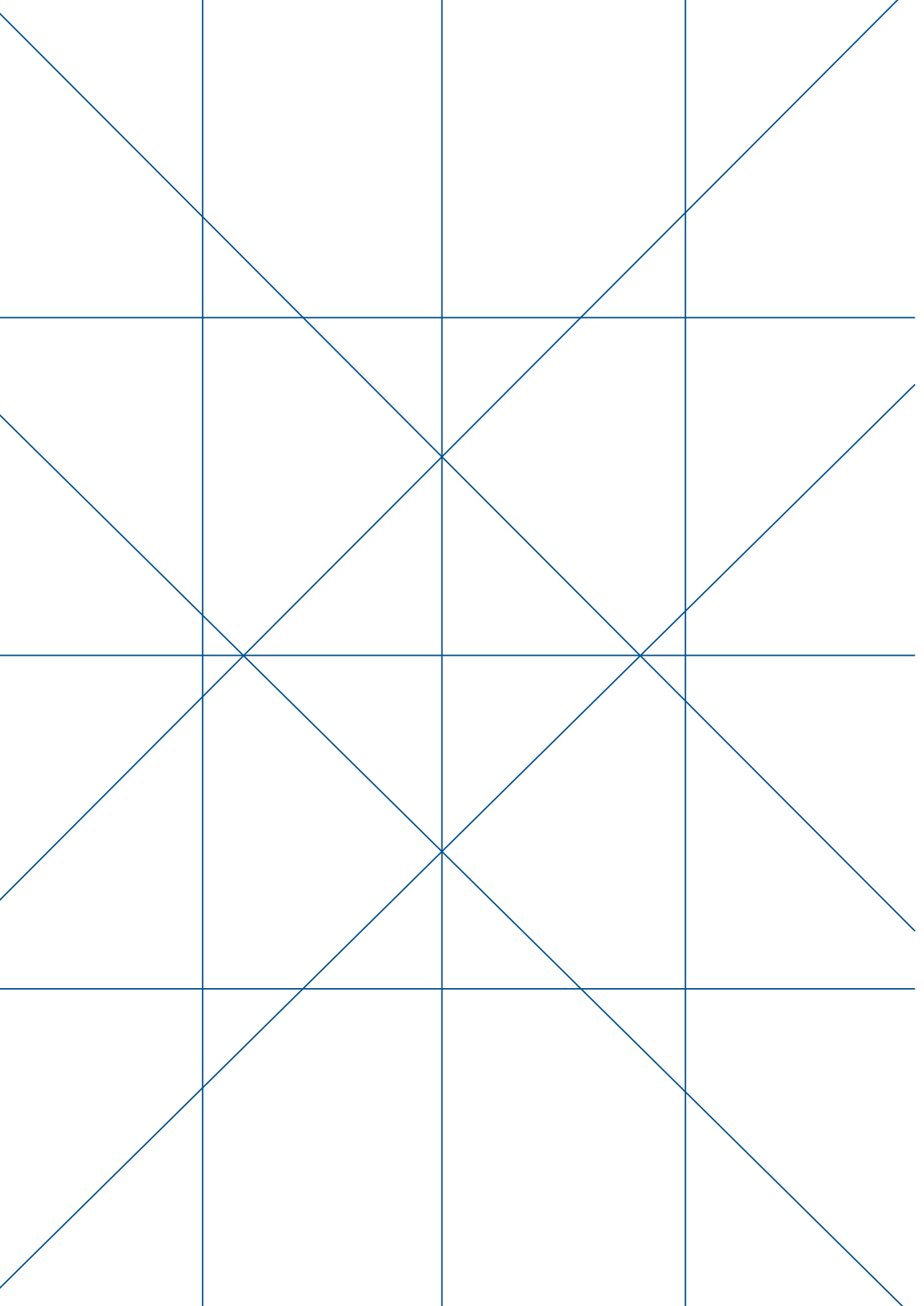
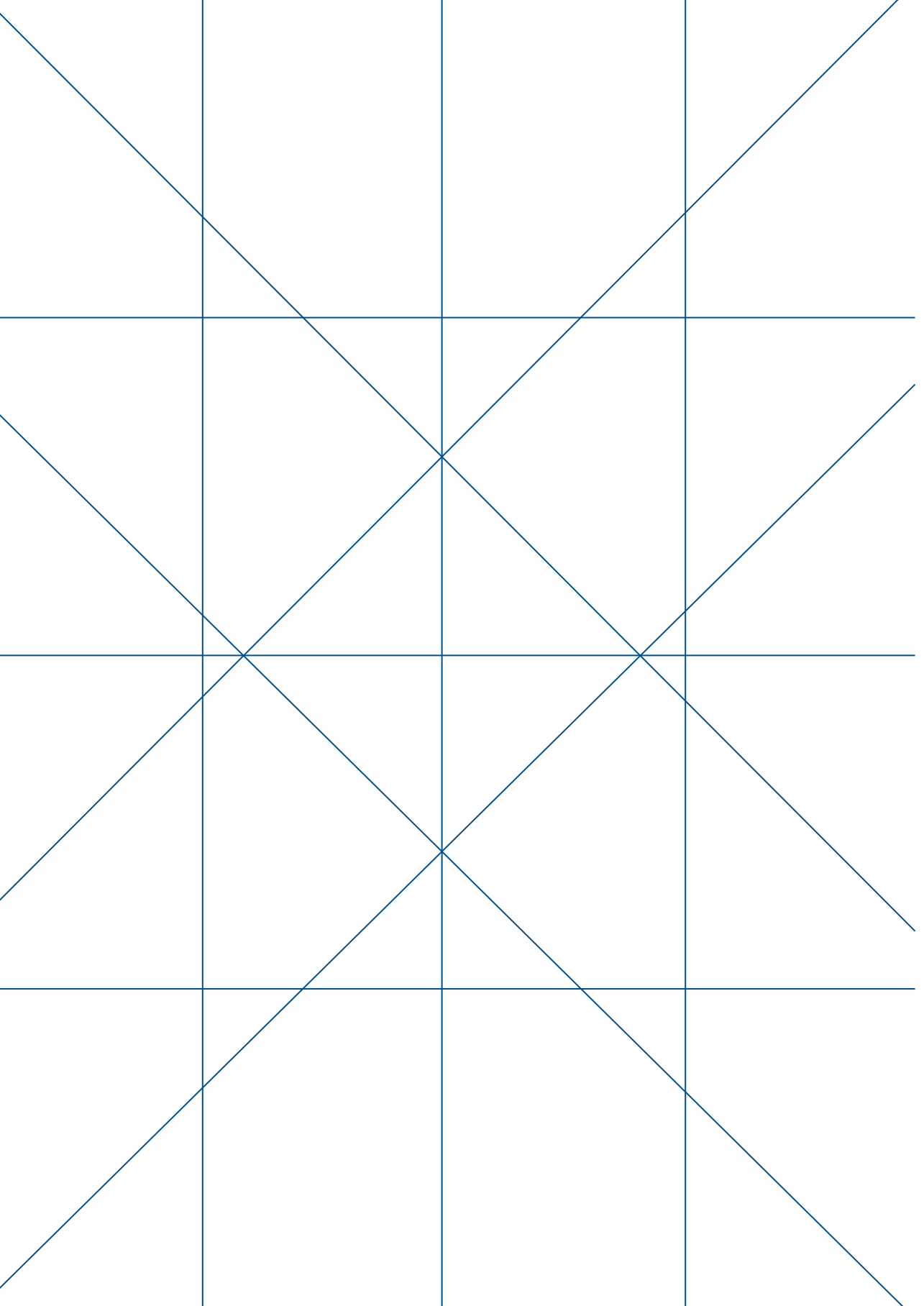


Part III

The Clinical Management of Abdominal Wall Hernias



Chapter 6

The prevention of incisional hernias

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Book Chapter

Introduction

Incisional hernia is a common occurring long-term complication following midline laparotomies, with a weighted mean rate at 2 years of 13% [1]. Recent randomized controlled trials show an incidence of 21-30% [2, 3]. In high-risk patients, including patients with an abdominal aortic aneurysm and high BMI ≥ 27, the incidence is estimated up to 69% after long-term follow-up [4]. Risk factors for the development of incisional hernia may be divided into patient-related risk factors and surgery-related risk factors. Patient-related risk factors are male sex, older age, smoking, malnourishment, poor diabetic control, coughing, use of steroid drugs, abdominal aortic aneurysm, malignancy, and history of chemotherapy. Also, impaired wound healing and reduced ratio of collagen type I/III are known risk factors. Surgical factors are the type of laparotomy incision (midline, transverse, or paramedian), operative status (elective or emergency), and peri- or postoperative wound problems, together called surgical site occurrence such as seroma formation, wound dehiscence, and surgical site infections [5]. An incisional hernia may cause obstruction and strangulation of the bowel, which can result in emergency surgery, with associated morbidity and mortality. Moreover, pain, discomfort, and cosmetic complaints caused by an incisional hernia may result in an impaired quality of life [6]. Additionally, the 10-year recurrence rates after incisional hernia repair are estimated up to 64% after primary repair and 32% with mesh repair [7]. Furthermore, incisional hernias do not only affect patients' health, it also creates a financial burden for public health. Optimizing surgical techniques and used materials to close abdominal wall incisions holds the potential of preventing the development of incisional hernias, reducing postoperative disability, and saving costs in the healthcare system. The prevention of incisional hernias is of paramount importance at both the individual and socioeconomic level. The surgical techniques and used suture materials for closing abdominal wall incisions are important determinative factors in preventing an incisional hernia and will be discussed in this chapter. Finally, the use of a prophylactic mesh placement for the prevention of incisional hernias and optimization of patients pre-, peri-, and postoperatively will be discussed.

Suturing technique

In the first-century AD, Aulus Cornelius Celsus was the first to document about the significance of surgical closure of the abdominal wall. A century later, the Greek surgeon Galen of Pergamon wrote about the mass closure of the abdominal wall. He also suggested to enter the abdominal cavity by paramedian incisions where possible in order to prevent incisional hernias. In the Middle Ages (AD 500-1500) scientific knowledge in hernia prevention and repair was mostly lost. In the nineteenth century, abdominal surgery became more common and survivable due to the discovery of asepsis and general and local anesthesia. In the last century, Read and other researchers focused on a collagen disorder as an explanation for hernia formation, which is called herniosis. On the other hand, another surgeon, Jenkins, pondered upon the mechanical cause of the development of incisional hernias. After surgery, an abdominal girth and the xiphoid - pubic distance may lengthen up to 30% during abdominal distension [8]. To allow this lengthening to occur and ensure a minimal rise in tension between the sutures and the tissues, an adequate reserve of suture length is necessary. A suture length (SL) to wound length (WL) ratio of 4:1 is calculated based on an increase of 30% of the wound length due to postoperative abdominal distension. Various clinical studies have shown that the suture length to wound length ratio of < 4 resulted in a higher incidence of incisional hernias after midline laparotomy and a suture length to wound length ratio of ≥ 4 is recommended after midline laparotomy (Figure 1) [9] [10]. Besides a suture length to wound length ratio of ≥ 4, it is recommended to use a continuous technique (versus interrupted) with slowly or nonabsorbable sutures (versus rapidly absorbable) as shown in various meta-analyses [11] [12]. In addition, continuous suturing is significantly faster to perform. The Swedish research group of Israelsson has developed the small bites technique (stitches 5-8 mm from the wound edge while only including the aponeurosis in the stitches) for the closure of midline incisions. A continuous, single-layer monofilament suture closed the incision, and self-locking anchor knots were used in this study. This technique was confirmed in the STITCH trial, which is a recent randomized controlled study, where the common conventional large bites technique (*i.e.*, 10 mm every 10 mm from the wound edge; long stitch) was compared with the small bites technique (*i.e.*, 5 mm every 5 mm from the wound edge; short stitch) (Figure 2). After a

follow-up of 1 year, it is shown that the small bites suture technique is more effective for the prevention of incisional hernia in midline incisions, without a higher rate of adverse events [2]. Moreover, single, aponeurotic layer closure is recommended in elective midline abdominal wall incisions. However, suturing all layers separately and peritoneal closure is not recommended [13]. In the European Hernia Society (EHS) guidelines, it is recommended to avoid midline incisions if possible. The occurrence of incisional hernias after both transverse and paramedian incisions are significantly lower compared with midline abdominal wall incisions, but without a difference in burst abdomen rates [14]. However, a midline incision is still the most common used incision to access the abdominal cavity. This type of incision allows the surgeon to be quick and provides an expansive view of the abdominal cavity, with minimal harm to the nerves, vessels, and muscles.

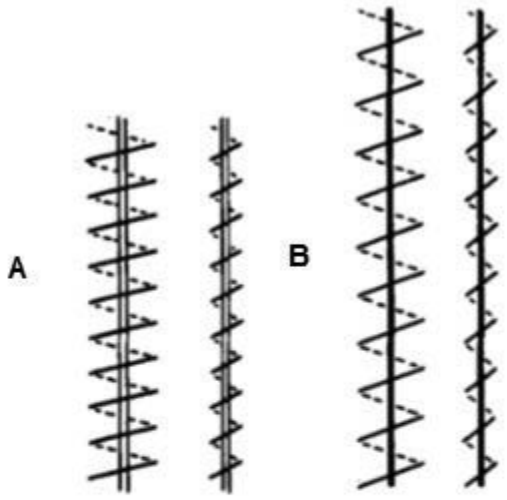

Figure 1. Suture length to wound ratio (A) and suture length to wound ratio after 30% abdominal distension (B). Source: Adapted from Jenkins TP. The burst abdominal wound: a mechanical approach. Br J Surg. 1976;63(11):873-6

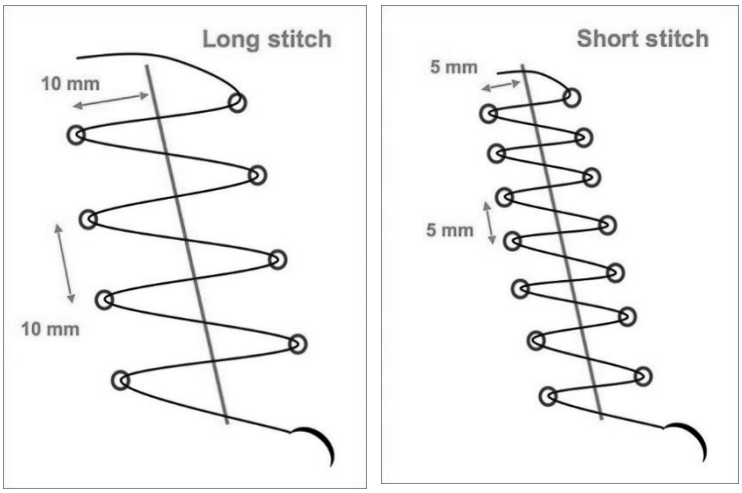

Figure 2. Large bites technique with long stitch (A) and small bites technique with short stitch (B) Source: Meijer E-J et al. The principles of Abdominal Wound Closure. Acta Chir Belg 2013;113(4):239-244.

Suture materials

The rapid growth in abdominal surgery over the past centuries has led to a rising global demand for suture materials. The Roman Galen of Pergamon is considered the first person to have used catgut sutures. Catgut sutures were fabricated by the twisted intestines of herbivorous animals and are degradable in the human body by proteolytic enzymes in approximately 90 days. In earlier days, silk and cotton were used when non-absorbable material was needed. During and after the Second World War, stainless wire and polymers were constructed. Now, various suture materials are available, i.e., braided versus monofilament and rapidly, slowly, versus nonabsorbable materials. Using a slowly or nonabsorbable suture to suture the fascia seems more reasonable compared to rapidly absorbable materials, since fascia healing needs at least 14 days to recover its strength. Using a fast-absorbable suture will not provide long enough support during fascia healing [15]. Fascia healing can be divided into three phases. The first exudative phase starts with recruiting inflammatory cells. In the proliferation phase, the fascia gains tensile strength via fibroblast proliferation and starts producing collagen. Mainly collagen type III is produced, which will be replaced by strong and thick type I collagen in the maturation phase. No significant differences between

a slow-absorbable suture material (polydioxanone) and a nonabsorbable suture material (polypropylene, Prolene) are found. However, nonabsorbable suture is associated with increased incidence of prolonged wound pain and suture sinus formation, which can possibly lead to long-term wound care and reoperation. Overall, these results indicate that using slowly-absorbable suture material is the most wise choice [11], [16-18]. Sutures impregnated with antibiotics, for example, with triclosan, have been postulated in order to decrease the rate of surgical site infection, which is a well-known risk factor for the development of incisional hernias. In a randomized controlled trial performed by Diener and colleagues, sutures impregnated with triclosan were compared with sutures without coating, and no significant difference in the rate of surgical site infections was shown [19]. Similarly, this outcome is supported by another recent meta-analysis. Henriksen and colleagues did not find a significant decrease in surgical site infections when triclosan-coated sutures were used for abdominal fascial closure. In the same study, a significant decrease in surgical site infections was seen when triclosan-coated Vicryl (absorbable) sutures were used. However, absorbable sutures are not recommended as discussed earlier in this chapter [20]. In addition, the cause of a surgical site infection after midline laparotomy is multifactorial, and suture material is only one possible contributing parameter. In the guidelines for the closure of the abdominal wall by the European Hernia Society, it is not advised to use sutures impregnated with antibiotics since no data is available on the development of incisional hernias [14]. Also, it is recommended to use monofilament suture materials, because those are associated with a lower surgical site infection rate compared with multifilament sutures [21]. In conclusion, a continuous, single aponeurotic layer with slowly-absorbable monofilament sutures is recommended for the closure of the fascia.

Surgical site infection

Surgical site infection (SSI) is a common complication, occurring between 3% and 40% after surgery and associated with increased morbidity, readmission rates, length of hospitalization, and healthcare costs. The highest SSI rates mostly occur after major abdominal and colorectal surgery. Moreover, SSIs are a well-known risk factor for the development of incisional hernias. It is shown

that patients with a SSI were two times more likely to develop an incisional hernia compared with patients without a SSI [22]. Various strategies are studied in order to prevent the occurrence of surgical site infections. Studied determinants were maintaining intraoperative normothermia, using barrier protectors or fresh closing trays in order to reduce bacterial load within the wound, euvolemia, and increasing perioperative oxygen tension, for example. However, single interventions do not reduce the occurrence of SSIs; bundling of interventions is required.

Prophylactic mesh augmentation

Since 1995 studies have been performed to prove the effect of prophylactic mesh augmentation after laparotomy. To date, a number of randomized studies have confirmed the effectiveness of the use of a prophylactic mesh for the closure of the abdominal wall in high-risk patients. There is growing evidence for prophylactic mesh augmentation for the prevention of incisional hernia. A recent example is the PRIMA trial; in this large international multicenter and randomized controlled trial, a comparison was made between preventive prophylactic onlay or sublay mesh reinforcement and primary closure with sutures in elective midline laparotomies [3]. This study was performed in patients with a higher risk of developing an incisional hernia, *i.e.*, patients in this study had either an abdominal aortic aneurysm or a body mass index of 27 kg/m² or higher. After a follow-up period of 2 years an incidence of incisional hernia of 30% was found in the non-mesh group, 13% in the onlay mesh group, and 18% in the sublay mesh group. Also, a recent meta-analysis confirmed that reinforcement of the abdominal wall by using a prophylactic mesh results in a decreased incidence of incisional hernias compared with primary repair with sutures [23]. Despite the strong evidence in the literature by now for the use of prophylactic mesh augmentation, several questions remain unanswered at present. Firstly, the exact patient population who will need a prophylactic mesh still needs to be determined. There is a variation in selected high-risk patients in the performed studies. Secondly, the optimal anatomical location for the placement of a mesh is still under discussion. Both locations, on- and sublay, are proven safe in the PRIMA trial. The onlay position is a less complex surgical technique compared with the sublay position. Nevertheless,

seromas are more frequently seen in patients with an onlay placed mesh, which is associated with a higher rate of surgical site infections. However, in the PRIMA trial, a higher rate in seromas did not result in an increased incidence of surgical site infections or other complications. On the other hand is the sublay position a technically more difficult surgical technique for surgeons that do not perform incisional hernia repair (*i.e.,* vascular surgeons, gynecologists, and urologists). An important question in this case is what risk of developing an incisional hernia legitimizes the placement of a prophylactic mesh. A better understanding of complication rates of a prophylactic mesh in contrast with the risk of developing an incisional hernia and patient selection is needed.

Patient optimization

Unfortunately, genetic susceptibility or connective tissue disorders are risk factors in the development of an incisional hernia, which cannot be influenced. On the contrary, numerous susceptible patient-related risk factors have been shown to play a major role in incisional hernia occurrence. Physicians should try to optimize modifiable risk factors such as smoking, obesity, malnutrition, glycemic levels, coughing, and use of steroid drugs. Obesity is a known factor for the occurrence of incisional hernia after laparotomy and also for recurrence after initial repair. Decreased vascularity of adipose tissue, leading to local hypoxia and impaired collagen synthesis may lead to impaired wound healing. Another factor is an increased intra-abdominal pressure resulting in more stress on the suture line. Although, obesity is a complex multifactorial disease and extremely difficult to affect, weight loss should be encouraged. On the contrary, malnourishment may result in more postoperative complications such as surgical site infections. Also, higher HbA1C than 7% is associated with an increase in infectious complications subsequently resulting in higher rates of incisional hernias [24]. Smoking is a well-known adversely influencing factor for tissue healing and should be strongly discouraged [25]. The use of steroids is a known risk factor for wound complications, and the need for steroids should be carefully reviewed pre- and postoperatively. Also, chronic pulmonary obstructive disease (COPD) should be well controlled preoperatively in order to reduce postoperative coughing, pneumonia, and steroid use.

Conclusion

Taken together, this chapter shows the complexity of the prevention of an incisional hernia. The two important determinants emerged from this chapter for the prevention of an incisional hernia are surgical techniques and susceptible patient-related characteristics. Surgical techniques such as suture length to wound length ratio, consequently the stitch size and suture materials are influential for the development of an incisional hernia. Modifiable patient-related risk factors include for example obesity and smoking. In order to prevent an incisional hernia, these risk factors and surgical techniques should be optimized based on recently published guidelines.

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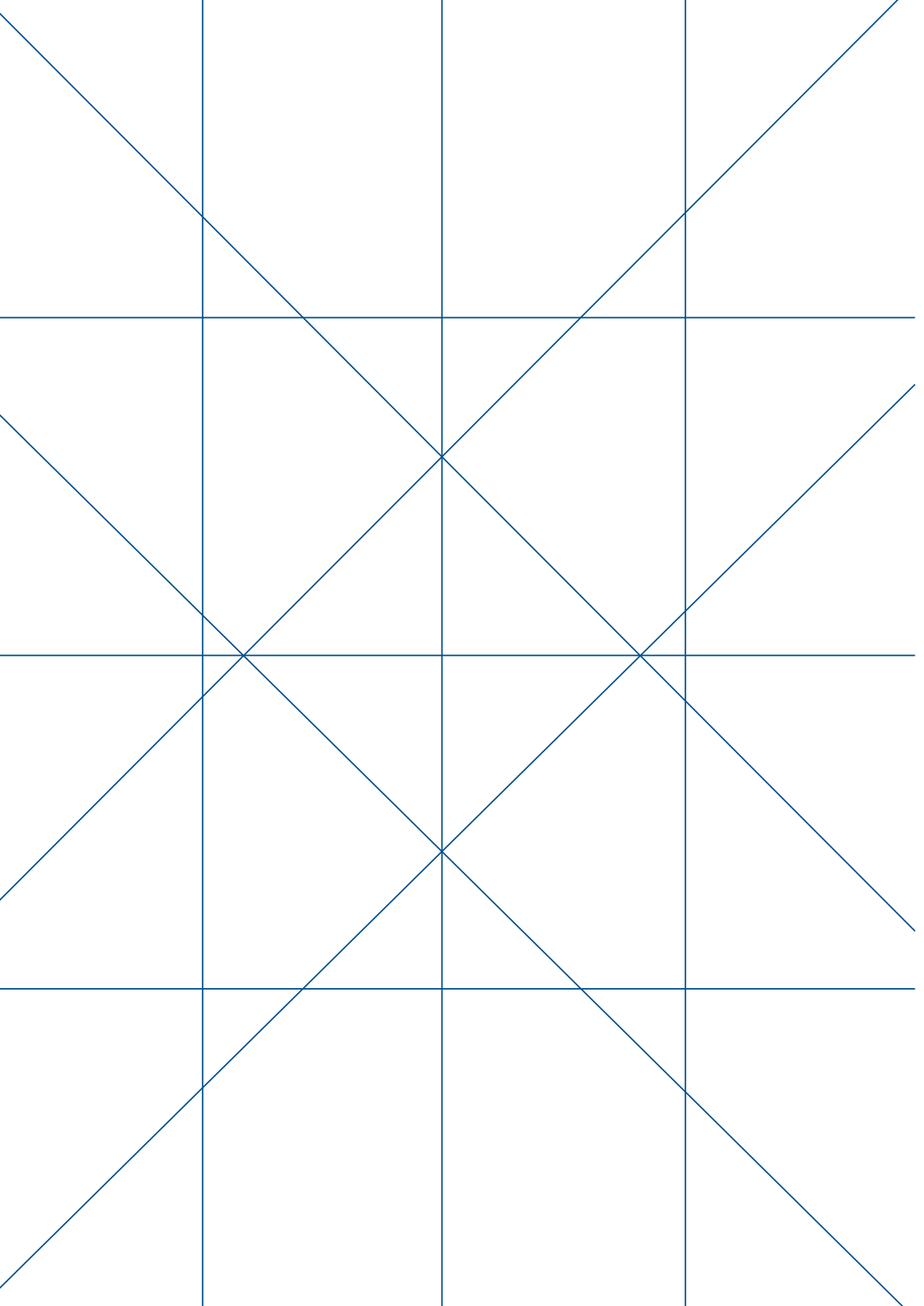

Chapter 7

Risk factors for incarceration in patients with primary abdominal wall and incisional hernias, a prospective study in 4,472 patients

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Abstract

Background

Incarceration of primary and incisional hernias often results in emergency surgery. The objective of this study was to evaluate the relation of defect size and location with incarceration. Secondary objectives comprised identification of additional patient factors associated with an incarcerated hernia.

Methods

A registry-based prospective study was performed of all consecutive patients undergoing hernia surgery between September 2011 and February 2016. Multivariate logistic regression was performed to identify risk factors for incarceration.

Results

In total, 83 (3.5%) of 2352 primary hernias and 79 (3.7%) of 2120 incisional hernias had a non-reducible incarceration. For primary hernias, a defect width of 3–4 cm compared to defects of 0–1 cm was significantly associated with an incarcerated hernia (OR 2.85, 95% CI 1.57–5.18, $p=0.0006$). For incisional hernias, a defect width of 3–4 cm compared to defects of 0–2 cm was significantly associated with an incarceration (OR 2.14, 95% CI 1.07–4.31, $p=0.0324$). For primary hernias, defects in the peri- and infra-umbilical region portrayed a significantly increased odds for incarceration as compared to supra-umbilical defects (OR 1.98, 95% CI 1.02–3.85, $p=0.043$). Additionally, in primary hernias age, BMI, and constipation were associated with incarceration. In incisional hernias age, BMI, female sex, diabetes mellitus and ASA classification were associated with incarceration.

Conclusion

For primary and incisional hernias, mainly defects of 3–4 cm were associated with incarceration. For primary hernias, mainly defects located in the peri- and infra-umbilical region were associated with incarceration. Based on patient and hernia characteristics, patients with increased odds for incarceration may be selected and these patients may benefit from elective surgical treatment.

Introduction

Abdominal wall hernias may result in pain, discomfort and aesthetic dissatisfaction and remain an important surgical challenge [1]. Moreover, hernias may be associated with significant morbidity and in rare cases mortality due to incarceration of bowel or abdominal contents such as fat or omentum [2-4]. Incarceration of the bowel is an absolute indication for emergency surgery. Previous research has shown prevalence rates of 4–15% of abdominal wall hernias resulting in emergency surgery. Emergency surgery is associated with severely compromised outcomes and increased mortality as compared to elective hernia repair [2, 3, 5, 6].

Risk of incarceration may be increased due to factors increasing intra-abdominal pressure. Obesity, ascites, chronic cough, and constipation are factors that all have been reported to increase intra-abdominal pressure [4, 7-9]. Hernia characteristics such as defect location and defect size may be associated with incarceration as well. Smaller defects are often thought to be at increased risk for incarceration; however, the evidence supporting this theory is limited. In fact, a previous study found no evidence for an increased incarceration risk in defects below 2 cm and another recent study found no association at all between defect size and hernia incarceration [4, 6].

The primary objective of this prospective study was to evaluate the relation of defect size and location with incarceration in primary and incisional hernias. Secondary objectives comprised identification of additional patient factors associated with an incarcerated hernia.

Methods

This prospective study was conducted within the French Hernia-Club registry. The Hernia-Club registry is approved by the French ‘Commission Nationale de l’Informatique et des Libertés’ (CNIL registration number: 1993959v0). Since this study is registry based and guaranties completely anonymized data, additional participant and institutional review board approval were not required according to the Dutch and French national standards. This study was conducted according to the STROBE (Strengthening the Reporting of Observational studies in Epidemiology) recommendations for observational studies [10].

Study design

A registry-based prospective study was performed including all adult patients in the French Hernia-Club registry that underwent hernia repair surgery, for primary or incisional hernias, between September 1, 2012 and February 29, 2016. Patients with incarcerated hernias were compared to patients without an incarcerated hernia. The present study differentiates between two types of incarceration as determined during surgery. The first type constitutes of a non-reducible protrusion of abdominal contents (e.g. fat, omentum, or bowel) through the abdominal wall defect. A hernia was considered non-reducible if reintegration of contents was only possible after adhesiolysis or enlarging of the defect. The second type constitutes of incarcerated hernias that could be easily manually reduced without the need for adhesiolysis or enlargement of the defect. Only the first type of incarceration, i.e. non-reducible incarceration was considered as endpoint for the present analysis. Cases without information on incarceration were considered as non-informative and subsequently excluded from further analysis.

Hernia-club registry

The Hernia-Club registry is a prospective and anonymized online database of all surgical procedures for primary and incisional hernias. The registry contains data of abdominal wall surgery performed in academic and non-academic centres by 47 surgeons. Each participating specialist must accept and sign the Charter of Quality. This states that: ‘all input must be registered in a consecutive, unselected and exhaustive manner and in real time.’ Data from screening, pre-, peri- and postoperative periods are collected in real time through online forms by the operating surgeon. A total of 164 parameters are collected. To ensure high-quality data, participants consent to random peer review of the original medical charts. Within a follow-up period of 2 years, outcomes are collected by the surgeon and further checked by an independent research associate. In case of discrepancies in collected data, the medical records are checked. The collected parameters in this database are fully compatible with the European Hernia Society (EHS) classification of primary and incisional abdominal wall hernias and the European Registry of Abdominal Wall Hernias (EuraHS) international online platform [11, 12].

Data collection

For the present study, predefined patient baseline characteristics and hernia characteristics were extracted from the Hernia-Club registry. Baseline characteristics of interest comprised age, body mass index (BMI), sex, current smoking habits, diabetes mellitus, corticosteroid use, radiotherapy, chemotherapy, history of abdominal aortic aneurysm (AAA), collagen disorder, anticoagulant use, history of abdominal hernia (inguinal, primary or incisional), family history of abdominal hernia, American Society of Anesthesiologists (ASA) score, and primary surgery (none, gastro-intestinal, gynaecologic, or other). Factors of interest related to increased intra-abdominal pressure comprised ascites, chronic cough, constipation (i.e. frequent episodes of no defecation lasting for more than 3 days), and heavy lifting (i.e. patients who have to carry more than 10 kg multiple times a day). Hernia characteristics comprised hernia type (primary or incisional), defect location (supra-umbilical, (peri)-umbilical, infra-umbilical, or lateral), defect width, recurrent hernia, and previous surgery with mesh. Data on defect width was measured either by physical examination alone or by physical and radiological examination. Defect width was only available in whole centimetres. Defect width was categorized in 4 categories for primary hernias (1 cm, 2 cm, 3–4 cm, ≥5 cm) and for incisional hernias (1–2 cm, 3–4 cm, 5–10 cm, >10 cm).

Statistical analysis

Statistical analysis was performed with RStudio (Version 1.0.153—© 2009–2017 RStudio, Inc.) [13]. Data on primary and incisional hernias were analysed separately. Categorical variables are presented as absolute numbers and percentages. Continuous variables are presented as means with corresponding standard deviations (SD). Missing data is presented in absolute numbers and percentage for each variable of interest in the Supplement. Normality of continuous variables was assessed with Levene's test for the equality of variances and graphically in histograms. Differences between incarcerated and non-incarcerated hernia patients were assessed with appropriate statistical tests including the Student's T test or Mann–Whitney U test for continuous variables and the Fishers' exact test or Chi-square test for categorical variables. To prevent bias, multiple imputations were performed to compensate for missing data. Multiple imputations were performed with five imputations to

ensure maximized use of available data. Factors potentially associated with incarceration were assessed in univariate logistic regression. Factors that were potentially related after univariate analysis ($p < 0.2$) and factors of clinical interest were considered for multivariate analysis. Factors with a strong mutual correlation were not fitted simultaneously. Linearity of continuous variables was graphically assessed. A 'full model' containing all variables of interest was reduced, based on the Wald-statistic and backward elimination, to include only those variables that improved discrimination. Defect width was not linearly associated with incarceration and was therefore not fitted as a continuous variable in a separate model. We deviated from the size categories provided by the EHS classification of primary and incisional abdominal wall hernias, since this classification did not provide enough leniency to adequately include small defects in the logistic regression model. Additionally, the EHS classification on defect location was simplified to include less categories to prevent overfitting of the logistic regression models. To prevent overfitting, a maximum of one variable was fitted per approximately ten incarceration events in the final model [14]. Discrimination of the final model was evaluated with the area under the receiver operator characteristic (ROC) curve [15]. A p-value of < 0.05 was considered statistically significant.

Results

A total of 2352 patients with a primary hernia and 2120 patients with an incisional hernia had data available on incarceration and were subsequently included in this study. In total, 83 (3.5%) of patients with a primary hernia had a non-reducible incarceration, another 106 (4.5%) had a reducible incarceration. In total, 79 (3.7%) of the patients with an incisional hernia had a non-reducible incarceration, another 93 (4.4%) had a reducible incarceration. The overall proportion of missing data was low: 1.6% of data was missing throughout the database. The exact number of missing data for each variable is presented in the Supplement. Patient baseline characteristics and hernia characteristics, as well as results after univariate logistic regression, are presented in Tables 1 and 2.

Variable Patient baseline characteristics	Not incarcerated N (%)	Incarcerated N (%)	Odds ratio OR (95% CI)	p-value
Total # patients	2269	83		
Age (years) *	55.4 ± 14.6	60.0 ± 17.4	1.02 (1.01-1.04)**	**0.0084**
BMI (kg/m²) *	27.8 ± 6.1	30.3 ± 7.5	1.06 (1.02-1.09)**	**0.0004**
Sex = female	886 (39.0)	35 (42.2)	1.14 (0.73-1.77)	0.57
Current smoking	514 (23.1)	12 (15.2)	0.60 (0.32-1.12)	0.11
Diabetes Mellitus	136 (6.1)	8 (9.6)	1.63 (0.77-3.46)	0.20
Corticosteroid use	76 (3.4)	4 (4.8)	1.38 (0.49-3.85)	0.54
Radiotherapy	19 (0.8)	2 (2.4)	2.81 (0.64-12.26)	0.17
Chemotherapy	28 (1.2)	2 (2.4)	1.67 (0.38-7.30)	0.49
History of AAA	6 (0.3)	0 (0)	-	0.83
Anticoagulant use	184 (8.2)	12 (14.5)	1.88 (1-3.54)	0.05
History of abdominal wall hernia	309 (13.7)	12 (14.5)	1.03 (0.55-1.92)	0.92
History of inguinal hernia	213 (9.4)	9 (10.8)	1.14 (0.56-2.30)	0.73
Family history of hernia	102 (4.5)	1 (1.2)	0.25 (0.03-1.84)	0.17
ASA classification				
I-II	1912 (84.9)	58 (70.7)	1 (reference)	
III-IV	340 (15.1)	24 (29.3)	2.35 (1.44-3.83)	**0.0006**
Ascites	17 (0.8)	3 (3.7)	4.48 (1.25-16.08)	**0.0215**
Chronic cough	107 (4.8)	2 (2.4)	0.55 (0.14-2.18)	0.39
Constipation	65 (2.9)	7 (8.5)	3.04 (1.34-6.90)	**0.0078**
Heavy lifting	225 (10.0)	11 (13.4)	1.36 (0.71-2.61)	0.35
Hernia Characteristics				
Defect location				
Supra-umbilical	526 (23.6)	11 (13.3)	1 (reference)	
Peri- and infra-umbilical	1659 (74.3)	70 (84.3)	2.04 (1.07-3.89)	**0.03**
Lateral	46 (2.1)	2 (2.4)	1.78 (0.37-8.63)	0.48
Defect width (cm)				
1	1328 (58.9)	40 (48.2)	1 (reference)	-
2	665 (29.5)	19 (22.9)	0.95 (0.54-1.65)	0.84
3-4	205 (9.1)	22 (26.5)	3.31 (1.91-5.74)	**<0.0001**
≥ 5	56(2.5)	2 (2.4)	1.38 (0.32-5.92)	0.66

Table 1. Primary hernias: patient baseline and hernia characteristics. Statistically significant values ($p < 0.05$) are given in bold.
BMI body mass index, *AAA* abdominal aortic aneurysm, *ASA score*: American Society of Anesthesiologists score
*Mean ± SD are presented for age and BMI; **per one increase; P for Wald-statistic after univariate logistic regression

Variable Patient baseline characteristics	Not incarcerated N (%)	Incarcerated N (%)	Odds ratio OR (95% CI)	p-value
Total # patients	2041	79		
Age (years) *	62.7 ± 14.1	67.9 ± 13.7	1.03 (1.01-1.05)**	**0.0013**
BMI (kg/m²) *	29.3 ± 6.1	32.1 ± 7.9	1.06 (1.03-1.09)**	**0.0002**
Sex = female	1050 (51.4)	59 (74.7)	2.78 (1.66-4.66)	**<0.0001**
Current smoking	365 (18.8)	10 (13.5)	0.73 (0.39-1.37)	0.33
Diabetes Mellitus	240 (12)	24 (31.6)	3.40 (2.07-5.57)	**<0.0001**
Corticosteroid use	73 (3.6)	2 (2.6)	0.71 (0.17-2.98)	0.64
Radiotherapy	36 (1.8)	1 (1.3)	0.74 (0.10-5.16)	0.75
Chemotherapy	126 (6.3)	3 (3.9)	0.64 (0.20-2.01)	0.44
History of AAA	15 (0.7)	1 (1.3)	1.81 (0.23-14.35)	0.58
Anticoagulant use	341 (17)	16 (21.1)	1.30 (0.74-2.29)	0.37
History of abdominal wall hernia	844 (41.6)	35 (44.9)	1.15 (0.73-1.82)	0.54
History of inguinal hernia	215 (10.6)	5 (6.4)	0.56 (0.22-1.40)	0.21
ASA classification				
I-II	1418 (69.7)	33 (43.4)	1 (reference)	
III-IV	617 (30.3)	43 (56.6)	3.04 (1.89-4.89)	**<0.0001**
Primary surgery				
Gastro-intestinal	972 (48.2)	27 (35.5)	0.79 (0.45-1.40)	0.42
Gynecologic	344 (17.1)	25 (32.9)	2.12 (1.18-3.79)	**0.0118**
Other	700 (34.7)	24 (31.6)	1 (reference)	
Ascites	14 (0.7)	0 (0)	-	0.85
Chronic cough	196 (9.7)	8 (10.4)	1.12 (0.54-2.30)	0.76
Constipation	131 (6.5)	11 (14.3)	2.33 (1.2-4.51)	**0.0122**
Heavy lifting	139 (6.9)	8 (10.4)	1.57 (0.74-3.33)	0.07

Variable	Not incarcerated N (%)	Incarcerated N (%)	Odds ratio OR (95% CI)	p-value
Hernia characteristics				
Type of hernia				
Recurrent hernia	410 (20.4)	21 (28.0)	1.63 (0.95-2.77)	0.07
Previous surgery with mesh	689 (34.2)	20 (26.7)	0.74 (0.44-1.25)	0.26
Defect location				
Supra-umbilical	359 (22.1)	9 (15.3)	1 (reference)	
Peri- and infra-umbilical	955 (58.7)	45 (76.3)	1.80 (0.88-3.68)	0.11
Lateral	288 (17.7)	5 (8.5)	1.08 (0.42-2.81)	0.87
Defect width (cm)				
0-2	567 (28.6)	11(14.7)	1 (reference)	-
3-4	632 (31.9)	34 (45.3)	2.62 (1.32-5.19)	**0.0057**
5-10	658 (33.2)	27 (36.0)	2.08 (1.02-4.27)	**0.0450**
> 10	124 (6.3)	3 (4.0)	1.32 (0.39-4.51)	0.66

Table 2. Incisional hernia: patient baseline and hernia characteristics
Statistically significant values ($p < 0.05$) are given in bold.
BMI body mass index, *AAA* abdominal aortic aneurysm, *ASA* score American Society of Anesthesiologists score.
*Mean ± SD are presented for age and BMI; **per one increase; P for Wald-statistic after univariate logistic regression

Primary abdominal wall hernia

Results of univariate analysis are presented in Table 1. In univariate analysis, increasing age, increasing BMI, ASA class III–IV, ascites, and constipation were associated with an incarcerated hernia. Additionally, peri- and infra-umbilical defects were associated with an incarcerated hernia. Compared to defects of 0–1 cm, a defect width of 3–4 cm (OR 3.31, 95% CI 1.91–5.74), $p < 0.0001$) was significantly associated with an incarcerated hernia. In fact, of all patients with a defect width of 3–4 cm, 22 of 227 (10%) presented with an incarcerated hernia. In multivariate analysis only age, BMI, sex, constipation, defect width, and defect location contributed significantly to discrimination between patients with and without an incarcerated hernia (Table 3). Compared to defects of 0–1 cm, in multivariate analysis, only a defect width of 3–4 cm (OR 2.85, 95% CI 1.57–5.18, $p = 0.0006$) and peri- and infra-umbilical defects (OR 1.98, 95% CI 1.02–3.85, $p = 0.043$) were significantly associated with an

incarcerated hernia. In multivariate analysis, ascites and ASA classification were not significantly associated with an incarcerated hernia. The area under the ROC curve for the multivariate model was 0.68.

Incisional hernia

Results of univariate analysis are presented in Table 2. In univariate analysis increasing age, increasing BMI, female sex, diabetes mellitus, ASA score III–IV, gynaecologic surgery, and constipation were associated with an incarcerated hernia. No specific defect location (supra-, peri- and infra-umbilical or lateral) was associated with an incarcerated hernia. Compared to defects of 0–2 cm, a defect width of 3–4 cm (OR 2.62, 95% CI 1.32–5.19, $p = 0.0057$) and a defect width 5–10 cm (OR 2.08, 95% CI 1.02–4.27, $p = 0.045$) were significantly associated with an incarcerated hernia. In multivariate analysis, only age, BMI, sex, diabetes mellitus, heavy lifting, ASA classification, and defect width contributed significantly to discrimination between patients that presented with and without an incarcerated hernia (Table 3). Compared to defects of 0–2 cm, in multivariate analysis, only a defect width of 3–4 cm was significantly associated with an incarcerated hernia (OR 2.14, 95% CI 1.07–4.31, $p = 0.0324$). In multivariate analysis, gynaecologic surgery, constipation, and defect location were not significantly associated with patients that presented with an incarcerated hernia. The area under the ROC curve for the multivariate model was 0.76.

	Coefficient	Odds ratio (95%CI)	p-value
Primary hernias			
Intercept	-6.1051	-	-
Age (years)	0.0167	1.02 (1-1.03)	**0.0421**
BMI (kg/m²)	0.0341	1.03 (1-1.07)	**0.0377**
Sex = female	0.2767	1.32 (0.83-2.09)	0.24
Constipation	0.934	2.54 (1.08-6.02)	**0.0335**
Defect location			
Supra-umbilical	Reference	1 (reference)	
Peri- and infra-umbilical	0.6844	1.98 (1.02-3.85)	**0.043**
Lateral	0.1506	1.16 (0.24-5.69)	0.85
Defect width (cm)			
1	Reference	1 (reference)	
2	-0.1703	0.84 (0.48-1.49)	0.56
3-4	1.0488	2.85 (1.57-5.18)	**0.0006**
≥ 5	0.0637	1.07 (0.24-4.83)	0.93
Incisional hernias			
Intercept	-8.5286	-	-
Age (years)	0.0251	1.03 (1.01-1.05)	**0.0122**
BMI (kg/m²)	0.0342	1.03 (1-1.07)	0.06
Sex = female	1.0431	2.84 (1.66-4.87)	**0.0001**
Diabetes Mellitus	0.8384	2.31 (1.37-3.91)	**0.0017**
Heavy lifting	0.9882	2.69 (1.17-6.16)	**0.0196**
ASA classification			
I-II	Reference	1 (reference)	
III-IV	0.8124	2.25 (1.34-3.78)	**0.0021**
Defect width (cm)			
0-2	Reference	1 (reference)	
3-4	0.7627	2.14 (1.07-4.31)	**0.0324**
5-10	0.569	1.77 (0.84-3.7)	0.13
> 10	0.1598	1.17 (0.33-4.15)	0.80

Table 3. Results of multivariate logistic regression.
Statistically significant values ($p < 0.05$) are given in bold.
BMI body mass index, *ASA score* American Society of Anesthesiologists score; P for Wald-statistic after multivariate logistic regression.

Discussion

In this large prospective study within the French Hernia-Club registry of patients with primary and incisional hernias, a number of factors were associated with patients that had presented with either an incarcerated primary or incisional hernia. For both primary and incisional hernias, a defect width of 3–4 cm portrayed the highest odds (OR 2.85 and OR 2.14, respectively) for an incarcerated hernia. Probably defects ≤2 cm in width would still be too small to facilitate substantial protrusion of abdominal contents in most cases, whereas larger hernias would be too large to cause for substantial strangulation. For primary hernias, periumbilical and umbilical defects were associated with an increased odds for incarceration (OR 1.98), defect location was not associated with incarceration for incisional hernias.

Findings of a previous prospective cohort study assessing factors associated with emergency surgery in patients with abdominal wall hernias are reasonably similar to the present results, finding female sex and age to be associated with emergency surgery [6]. In this same study, the relation between defect size and emergency surgery in incisional hernias was disconcordant with the present results. This is likely due to different size categories used in this report; all defects between 2 and 7 cm were grouped together. Another retrospective study evaluated hernia characteristics as risk factors for incarceration in patients with a primary or incisional hernia [4]. In contrast to the present results, this study did not report a significant association between defect size and incarceration. However, in this study, patients with a primary and incisional hernia were grouped together. Nonetheless, the aetiology of both conditions is likely to be different [16]. This discrepancy could likewise be caused due to the fact that defect width was fitted as a continuous variable in the multivariate logistic regression model, whereas, in the present analysis, this relation was not linear. The authors additionally found hernia sac height and angle between the hernia sac and abdominal wall (on CT-scan) to be associated with incarceration.

The present study additionally found numerous patient factors to be associated with incarceration for either primary or incisional hernias. Increased BMI was correlated with incarceration. Additionally, it is conceivable that factors increasing abdominal pressure including constipation and heavy lifting may

be associated with incarceration. Other variables found to be associated, including age and ASA classification, may be secondary effects to variables which are not available in this current database. For example, clinicians may be more reluctant to operate older patients with higher ASA classification, resulting in increased odds of these patients being operated in an emergency setting due to incarceration. Nevertheless, it is conceivable that frail patients are at increased odds for a complicated prognosis. Patients with an incisional hernia, female sex was associated with incarceration (OR 2.31); however, in primary hernias, this association was not present. The reason for this association remains unclear. Although previous studies failed to show a strong correlation between pregnancy and hernia occurrence, the increased odds for incarceration in women may be related to physiological changes in the abdominal wall secondary to pregnancy [17, 18].

A strangulated and non-reducible hernia is an absolute indication for emergency surgery and causes for increased morbidity and mortality [2, 3, 5, 6]. Patients with incarcerated hernias are hospitalized longer and suffer from increased rates of severe postoperative complications [2-4]. Moreover, rates of emergency hernia repair have been increasing in the USA over the past years [19]. This might be related to an overall increase in prevalence of abdominal hernias [4]. Therefore, data constituting the prevention of incarceration is important and may improve clinical care and decision making.

The present and previous reports suggest that incarceration is, to a certain extent, predictable based on patient factors, hernia characteristics, and CT-findings. Nevertheless, in order to better predict which patients may be at increased risk for incarceration, future prospective cohorts require inclusion of those patients treated conservatively, CT-scans for additional biometric evaluation, and inclusion of time to event data. This would ensure accurate depiction of the complete order of events.

Limitations

Although all data was collected prospectively in an exhaustive manner, results may be influenced by selection bias to a certain degree, given the observational study design. All included patients underwent hernia repair surgery. Patients

who were treated conservatively were not included in this registry. Therefore, causality of found associations cannot be confirmed. Additionally, this limits the current potential to make accurate probability estimates. Patients presenting in an emergency setting may not be operated by a dedicated hernia surgeon affiliated with the Hernia-Club registry and may be less likely to be included in the registry database. However, this will likely have non-differential effects on reported odds ratios. Nevertheless, this may cause for an underestimation of the reported prevalence of incarceration. The proportion of missing data was reasonably low and multiple imputations were used to ensure maximized use of available data. Inherently, it was not possible to provide exact reasons for missing data at case and variable level. Therefore, a risk of reporting bias cannot be completely excluded. To allow for better interpretation and adequate effect estimation, defect width was categorized. However, in reality, no strict cut-offs exist and these estimates will merely represent an approximation of the true effects.

Conclusion

For primary and incisional hernias, mainly defects of 3–4 cm were associated with incarceration. For primary hernias, mainly defects located in the peri- and infra-umbilical region were associated with incarceration. Probably defects of ≤2 cm in width would still be too small for substantial protrusion of abdominal contents in most cases, whereas larger hernias would be too large to cause for strangulation. Based on patient and hernia characteristics, patients with increased odds for incarceration may be selected and these patients may benefit from elective surgical treatment.

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Supplemental materials

Variable	Primary hernia		Incisional hernia	
	Not incarcerated	Incarcerated	Not incarcerated	Incarcerated
	N (%)	N (%)	N (%)	N (%)
Total N	2352 (100)	83 (3.5)	2041 (100)	79 (3.9)
Patient baseline characteristics				
Age	8 (0.4)	1 (1.2)	10 (0.5)	0 (0)
BMI	22 (1.0)	1 (1.2)	18 (0.9)	4 (5.1)
Sex = female	0 (0)	0 (0)	0 (0)	0 (0)
Current smoking	41 (1.8)	4 (4.8)	104 (5.1)	5 (6.3)
Diabetes mellitus	23 (1.0)	0 (0)	38 (1.9)	3 (3.8)
Corticosteroid use	23 (1.0)	0 (0)	38 (1.9)	3 (3.8)
Radiotherapy	23 (1.0)	0 (0)	38 (1.9)	3 (3.8)
Chemotherapy	23 (1.0)	0 (0)	38 (1.9)	3 (3.8)
History of AAA	12 (0.5)	0 (0)	11 (0.5)	1 (1.3)
Collagen disorder	12 (0.5)	0 (0)	11 (0.5)	1 (1.3)
Anticoagulant use	23 (1.0)	0 (0)	38 (1.9)	3 (3.8)
History of abdominal wall hernia	12 (0.5)	0 (0)	11 (0.5)	1 (1.3)
History of inguinal hernia	12 (0.5)	0 (0)	11 (0.5)	1 (1.3)
History of primary ventral hernia	12 (0.5)	0 (0)	11 (0.5)	1 (1.3)
History of incisional hernia	12 (0.5)	0 (0)	11 (0.5)	1 (1.3)
Family history of abdominal hernia	12 (0.5)	0 (0)	11 (0.5)	1 (1.3)
ASA-score	17 (0.7)	1 (1.2)	6 (0.3)	3 (3.8)
Primary surgery				
Gastro-intestinal	NA	NA	25 (1.2)	3 (3.8)
Gynaecologic	NA	NA	25 (1.2)	3 (3.8)
Other surgery	NA	NA	25 (1.2)	3 (3.8)
Factors related to intraabdominal pressure				
Ascites	17 (0.7)	1 (1.2)	20 (1.0)	2 (2.5)
Chronic cough	17 (0.7)	1 (1.2)	24 (1.2)	2 (2.5)
Constipation	17 (0.7)	1 (1.2)	24 (1.2)	2 (2.5)
Heavy lifting	17 (0.7)	1 (1.2)	24 (1.2)	2 (2.5)
Recurrent hernia	NA	NA	32 (1.6)	4 (5.1)
Previous surgery with mesh	NA	NA	25 (1.2)	4 (5.1)

Variable	Primary hernia		Incisional hernia	
	Not incarcerated	**Incarcerated**	**Not incarcerated**	**Incarcerated**
	N (%)	N (%)	N (%)	N (%)
Defect location				
Supra-umbilical	37 (1.6)	0 (0)	414 (20.3)	20 (25.3)
Peri- and infra-umbilical	37 (1.6)	0 (0)	414 (20.3)	20 (25.3)
Lateral	37 (1.6)	0 (0)	414 (20.3)	20 (25.3)
Defect Size (cm)				
0 - 2	15 (0.7)	0 (0)	60 (2.9)	4 (5.1)
3 - 4	15 (0.7)	0 (0)	60 (2.9)	4 (5.1)
5- 10	15 (0.7)	0 (0)	60 (2.9)	4 (5.1)
> 10	15 (0.7)	0 (0)	60 (2.9)	4 (5.1)
Postoperative outcomes				
Admission (days)	0 (0)	0 (0)	0 (0)	0 (0)
Emergency surgery	5 (0.2)	1 (1.2)	9 (0.4)	1 (1.3)
Any complication	80 (3.5)	3 (3.6)	50 (2.4)	2 (2.5)
Wound complication	62 (2.7)	3 (3.6)	33 (1.6)	1 (1.3)
Surgical complication	77 (3.4)	2 (2.4)	41 (2.0)	2 (2.5)
Medical complication	56 (2.5)	2 (2.4)	36 (1.8)	2 (2.5)
Clavien Dindo	102 (4.5)	3 (3.6)	105 (5.1)	7 (8.9)

Supplemental table 1. Overview of missing data
Legend: BMI: body mass index; AAA: abdominal aortic aneurysm; ASA-score: American society of anesthesiologists score; NA: not applicable

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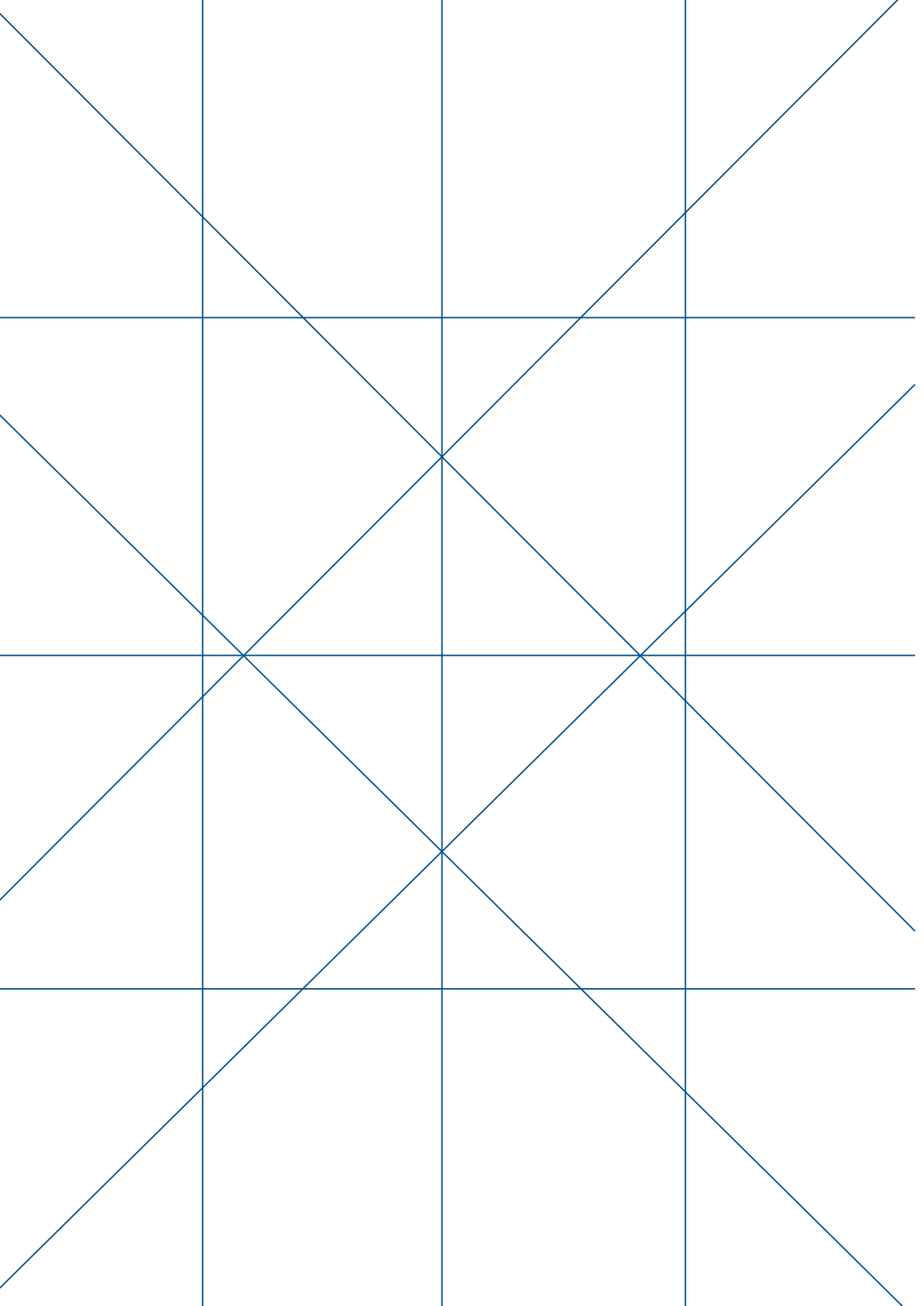

Chapter 8

Implementing preoperative Botulinum toxin A and progressive pneumoperitoneum through the use of an algorithm in giant ventral hernia repair

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Abstract

Background

Repair of large ventral hernias with loss of domain can be facilitated by preoperative Botulinum toxin A (BTA) injections and preoperative progressive pneumoperitoneum (PPP). The aim of this study is to evaluate the outcomes of ventral hernioplasty using a standardized algorithm, including component separation techniques, preoperative BTA and PPP.

Methods

All patients between June 2014 and August 2018 with giant hernias (either primary or incisional) of more than 12 cm width were treated according to a previously developed standardized algorithm. Retrospective data analysis from a prospectively collected dataset was performed. The primary outcome was closure of the anterior fascia. Secondary outcomes included complications related to the preoperative treatment, postoperative complications, and recurrences.

Results

Twenty-three patients were included. Median age was 65 years (range 28–77) and median BMI was 31.4 (range 22.7–38.0 kg/m^2). The median loss of domain was 29% (range 12–226%). For the primary and secondary endpoints, 22 patients were analyzed. Primary closure of the anterior fascia was possible in 82% of all patients. After a median follow-up of 19.5 months (range 10–60 months), 3 patients (14%) developed a hernia recurrence and 16 patients (73%) developed 23 surgical site occurrences, most of which were surgical site infections (54.5%).

Conclusion

Our algorithm using both anterior or posterior component separation, together with preoperative BTA injections and PPP, achieved an acceptable fascial closure rate. Further studies are needed to explore the individual potential of BTA injections and PPP, and to research whether these methods can prevent the need for component separation, as postoperative wound morbidity remains high in our study.

Introduction

One of the most prevalent complications after midline laparotomy is an incisional hernia [1]. Incisional hernias often require surgical repair as they may cause discomfort and pain [2]. G Giant hernias, which are more than 10 cm in width, or hernias with loss of domain (LOD) of more than 20%, in which the abdominal cavity is unable to fully accommodate the abdominal contents within its fascial boundaries, pose additional difficulties [3, 4]. In these hernias, closure of the fascia is impossible or will cause high pressure with a substantial risk of complications, such as abdominal compartment syndrome and pulmonary dysfunction [4]. Despite the risk of complications, surgical closure of a hernia with LOD might be indicated when quality of life is low. LOD can cause long-term disability, loss of core muscles, back pain, paradoxical respiratory motion, mesenteric edema, poor bowel function, skin necrosis, enterocutaneous fistula, and cosmetic issues [4]. For the repair of a giant hernia (with or without loss of domain), additional medialization of the rectus abdominis muscles might be required to achieve tension-free closure. Anterior or posterior component separation techniques (i.e. (modified) Ramirez [5] or transverse abdominis release (TAR)) can be used to obtain additional medialization of the rectus abdominis muscles [6]. In addition to component separation techniques, a progressive preoperative pneumoperitoneum (PPP) has shown to be a safe way to facilitate closure in hernias with LOD [7-10]. The use of PPP was first described by Goñi Moreno in 1947 [11]. PPP causes gradual expansion of the abdominal muscles and pneumatic lysis of adhesions in the abdominal cavity or hernia sac.

A more recent finding is that Botulinum toxin A (BTA) can be used to facilitate closure too, as it lowers the tension on the lateral abdominal muscles [12-14]. The combination of BTA and PPP, however, has been little described; the few studies that have been done suggest positive results [15]. This combination, however, is not always necessary for adequate repair. Additionally, PPP is rather expensive because it might require preoperative hospital stay [16].

A standardized preoperative strategy is required for patients with a giant hernia, as preoperative BTA and/or PPP can aid fascial closure, but their effects cannot be adjusted intra-operatively. This preoperative strategy would

ideally distinguish between patients with a giant hernia that [1] could be treated without preoperative aids, [2] patients in whom BTA alone would suffice, and [3] patients that would need the combination of BTA and PPP. As current literature is void of recommendations for use of these preoperative aides, an empirical algorithm was developed based on clinical experience. This retrospective analysis aimed to determine the closure rate of the anterior fascia aided by Botulinum toxin A and/or preoperative progressive pneumoperitoneum by the use of the algorithm, and could also serve as an evaluation of whether the algorithm is valuable in determining the need for these preoperative tools in specific patient groups. Secondary outcomes included complications related to the preoperative treatment, postoperative complications, and recurrences.

Methods

First, a preoperative strategy or algorithm for the treatment of complicated giant ventral hernias was developed in a large tertiary care university hospital in Ghent, Belgium. The algorithm was based on both hernia width and the presence or absence of loss of domain (Fig. 1). The rationale behind the algorithm was based on the primary goal of achieving anterior fascial closure after hernia repair. With this in mind, the interventions used in sequential fashion were (1) the gold standard retromuscular repair (Rives–Stoppa [17, 18]); (2) anterior component separation technique; (3) BTA injections; and (4) PPP. In hernias with a width of up to 10 cm, retromuscular repair was performed. The size of the defect at which the additional tool of anterior CST was added was set as 14 cm. BTA can be considered when the surgeon believes anterior fascia closure might still not be achievable despite the use of anterior CST, and from 18 cm hernia width, PPP can be considered to implement some “reserve” to prevent the surgeon from being unable to close the fascia intraoperatively. In large hernias over 22 cm of width, volume reduction and maximal medial advancement of the rectus muscles are desired; all tools are hypothesized to be needed in this specific complicated subset of patients. Approval of the Medical Ethics Committee was obtained prior to this study. Adult patients with an elective repair of a giant hernia, either primary or incisional, who presented between June 2014 and August 2018 were treated accordingly.

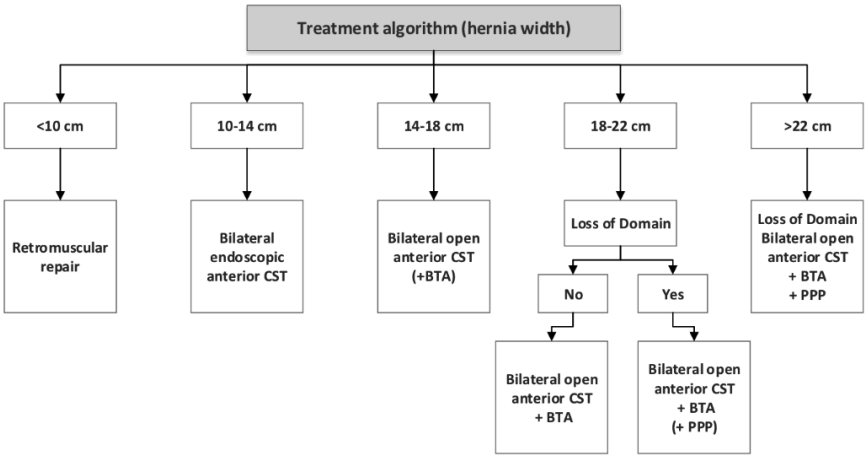

Figure 1. Treatment algorithm

As illustrated in Fig. 1, BTA injections (Botulinum toxin A, Allergan, Inc., Irvine, California) and PPP were administered to patients with a clinically estimated hernia width of more than 18 cm, thickened oblique muscles based on computed tomography (CT) examinations and/or a LOD≥20% based on volumetric measures on CT [19]. BTA injections were administered according to the protocol written by Zielinksi et al. [20]. BTA injections of 300 units dissolved in 150 cc 0.9% sodium chloride solution were given at three levels bilaterally. The injections were performed under ultrasound guidance by an experienced radiologist, using a Philips iU22 device equipped with a 3–9 MHz linear transducer and a biopsy guide. The injections were given into the transverse abdominal muscle, internal oblique, and external oblique muscle.

For PPP, after cardiopulmonary evaluation, a catheter (Medionics' Swan Neck Coil 2 cuff peritoneal dialysis, inner diameter of 2.6 mm and outer diameter of 5 mm) was placed through open surgery, under general anesthesia, subcostally in the right or left hypochondriac region at the day of admission. Up to 2 L of ambient air were insufflated into the abdominal cavity at day zero. On daily basis and until hernia repair, a variable amount of ambient air was insufflated into the abdominal cavity through a microporous filter, up until the point where the patient was no longer comfortable. All patients were hospitalized during

insufflation. Thromboprophylaxis (low molecular weight heparin, LMWH) at therapeutic dose was administered daily.

Mesh was used for all hernia repairs, which was fixated with continuous suture of Prolene 2-0.

Anterior fascial closure after hernia repair surgery took place with a running long-term absorbable polydioxanone suture 0, in a small step fashion with a small bite configuration. Suture length to wound length ratio was not measured.

Data collection

Retrospective data extraction from this prospectively collected data was performed. The following data were extracted from medical records: achievement of primary anterior fascial closure, baseline characteristics (age, gender, body mass index (BMI), smoking, medical history, and previous hernia surgery), hernia characteristics based on the EHS classification [21], data on the surgical procedure (ASA classification, surgery duration, type of repair, antibiotic prophylaxis, type and location of mesh), and follow-up time. Postoperative data in the form of postoperative complications, the surgical site occurrences (SSO), hernia recurrences, and reoperations were collected. A surgical site occurrence was defined as a surgical site infection (superficial, deep, mesh infection), seroma, hematoma, wound and fascia dehiscence, or enterocutaneous fistula formation. Information about BTA and PPP (side of the catheter (right or left), number of days for insufflation, amount of insufflated air) was collected. Additionally, the size of the hernia defect and volume of the hernia sac were measured from CT examinations before and after BTA and/or PPP, when available. The pre- and post-BTA abdominal muscle length was measured at the level of the mid-third lumbar vertebra and the inside of the abdominal wall. Measurements started at the paravertebral muscles and ended in the midline (or hernia) using post-processing analyses with SyngoVia Version VB20A (Siemens). All data were analyzed using SPSS ® Statistics for Windows, version 24.0.0.1, IBM corp. Armonk, NY.

Results

A total of 23 patients (12 males and 11 females), with a median age of 65 years (range 28–77 years) were treated between June 2014 and August 2018. Median BMI was 31.4 kg/m2 (range 22.7–43.3 kg/m2). Three patients (13%) were current smokers, 10 (43.5%) were ex-smokers, and 10 (43.5%) were non-smokers. Seven patients (30.4%) had diabetes mellitus. All patient characteristics are listed in Table 1.

Patient characteristics	**Overall N = 23**
Age, years, median (range)	65 (28-77)
Male (%)	12 (52.2)
BMI, kg/m² (range)	31.4 (22.7-43.3)
Smoking (%)	3 (13.0)
ASA Classification (%)	
II	14 (60.9)
III	9 (39.1)
Diabetes Mellitus (%)	7 (30.4)
Hypertension (%)	16 (69.6)
Cardiac disease (%)	9 (39.1)
Pulmonary disease (%)	8 (34.8)
Hepatic disease (%)	3 (13.0)
Renal disease (%)	0 (0)
History of malignant disease (%)	8 (34.8)
Corticosteroids use (%)	1 (4.3)
Primary hernia (%)	9 (39.1)
Recurrent hernia (%)	14 (60.9)
Number of previous herniotomies	
1	9 (39.1)
2	3 (13.0)
4	2 (8.7)

Table 1. Patient characteristics

BMI: body mass index, ASA: American Society of Anesthesiologists.

Hernia characteristics

Fourteen patients (60.9%) had a recurrent hernia and nine patients (39.1%) had a primary hernia. CT scans to evaluate preoperative loss of domain were available for 17 patients (73.9%). The median LOD was 29% (range 12–226%), based on hernia sac volume to abdominal cavity volume ratio.

BTA and PPP

Twenty patients (87%) received BTA injections with a median of 45 days before surgery (range 28–119 days). The median difference in muscle length on the right side pre- and post-BTA injections was 3.6 cm (cm) (range 0.4–7.6 cm) and on the left side 2.7 cm (0.7–7.9 cm). Seventeen patients (73.9%) underwent PPP. A median of 10.2 L of air, with a range of 6.4–19.1 L, was insufflated over a median period of 12 days (range 7–21 days). The insufflation of the abdominal cavity was initiated 14 days before surgery (median, range 5–43). The hernia sac volume (HSV) to abdominal cavity volume (ACV) ratio was 0.29 before BTA and/or PPP (median, range 0.12–2.26, 6 CT scans missing) and 0.33 after BTA and/or PPP (range 0.09–2.00, 6 CT scans missing). Fourteen patients (60.9%) received the combination of BTA injections and PPP. Data regarding patients having both BTA and PPP are summarized in Table 2. Several patients did not require both BTA and PPP based on their clinical presentation and our algorithm. For example, in case LOD was present without thickened lateral abdominal wall musculature, only PPP was administered preoperatively. When we evaluate the practical usefulness of our algorithm, in the hernia group with widths between 14 and 18 cm, the actually performed pre- and intra-operative treatment differed in seven out of nine patients (77.8%) from what was suggested according to the algorithm. In contrast, in all patients from both groups with hernias over 18 cm, the proposed surgical technique from the algorithm was used. Only three out of 14 patients in those two groups (21.4%) received different preoperative management than suggested by the algorithm. Details on the pre- and intraoperative operative treatment per treatment group from the algorithm are summarized in Table 3. Additionally, the hernia characteristics using the EHS classification are presented in Table 3 [21].

Treatment	Overall N = 23
BTA, number (%)	20 (87.0)
Days before surgery	45 (8-120)
Δ muscle length pre- and post-BTA, right (cm)	3.6 (0.4-7.6)
Δ muscle length pre- and post-BTA, left (cm)	2.7 (0.7-7.9)
PPP, number (%)	17 (73.9)
Side drain, right (%)	16 (94.1)
Total air (liters)	10.2 (6.4-19.1)
Total days of air insufflation	12 (7-21)
Days before surgery	14 (5-43)
HSV/ACV ratio before BTA and/or PPP	0.31 (0.12-2.26)
HSV/ACV ratio after BTA and/or PPP	0.33 (0.08-2.00)
BTA + PPP combination, number (%)	14 (60.7%)
Days before surgery, BTA	43 (8 - 120)
Δ muscle length pre- and post-BTA, right (cm)	4.3 (0.4 - 7.6)
Δ muscle length pre- and post-BTA, left (cm)	4.2 (1.3 - 7.9)
Days before surgery, PPP	14 (5 - 37)
Side drain, right (%)	13 (92.9)
Total air (L)	10.4 (6.4 - 19.1)
Total days of air insufflation	11 (7 - 21)

Table 2. BTA and preoperative progressive pneumoperitoneum
All values are median (range) or n (%). PPP: preoperative progressive pneumoperitoneum, HSV: hernia sac volume, ACV: abdominal cavity volume, Δ: difference in muscle length.
** Only 1 measurement available*

Complications of PPP and BTA

The administration of BTA injections did not result in complications. The use of PPP, however, resulted in complications in five patients. One patient had a cardiac arrest at day 5 of PPP and cardiopulmonary resuscitation was performed successfully. Post hoc evaluation showed an AV block grade II, with no signs of pulmonary or air embolisms. A PPP catheter was replaced approximately 2 weeks after the cardiac arrest. Consequently, the patient developed a liver hematoma, which was drained surgically. Another patient had a hematoma retro rectus at the site of the catheter during PPP, confirmed with a CT scan, which was drained during hernia repair. One patient was admitted to the

intensive care unit due to hemorrhagic shock based on an extensive hematoma after placement of the PPP catheter at day 5. This hematoma was drained surgically. One patient developed an enterocutaneous fistula during PPP. The fifth patient died preoperatively due to hemorrhage at the site of the bursa omentalis and multi-organ failure after 5 days of PPP, and was, therefore, not evaluated in further analyses (Fig. 2).

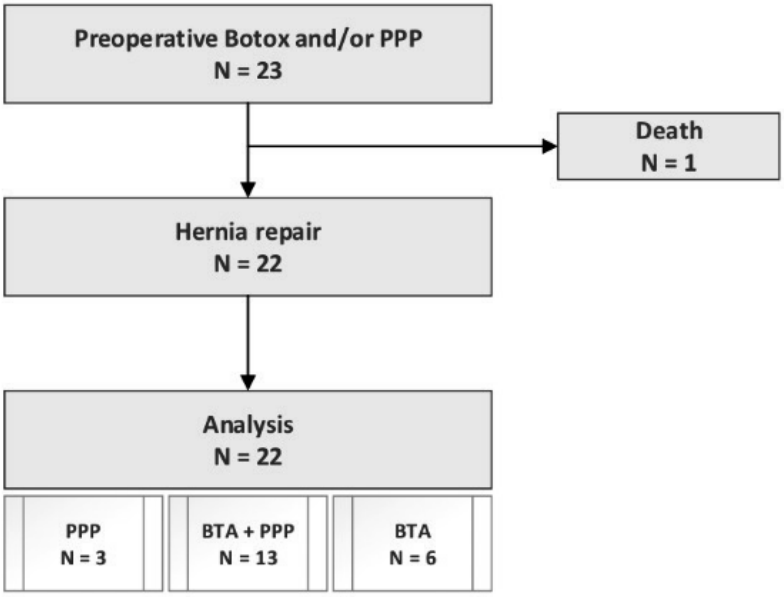

Figure 2. Flowchart data analysis

Surgical characteristics

All abdominal hernia repairs (N=22) were elective laparotomies. Hernia repair was performed by either anterior component separation or transversus abdominis release, except in one patient. This patient did not need component separation and could be repaired without this technique. Intra-operatively, the median length of the hernia was 20 cm (range 8–30 cm) and the median width was 21 cm (range 12–30 cm). Mesh localization was either intraperitoneal (N=17, 77.3%) or retromuscular (N=5, 22.7%). Median length of the meshes used was 42 cm (range 28–50 cm) and median width was 32 cm (range 26–38 cm). Median mesh surface (length × width) was 1344 cm2(range 572–1850 cm2). All patients were clinically re-evaluated in July 2019. The follow-up period, therefore, ranged from 10 to 60 months, with a median follow-up of 19.5 months. All surgical characteristics can be found in Table 3.

Hernia width	**Width 14-18 cm**	**Width 18-22 cm**	**Width >22 cm**
	N = 9	**N = 6**	**N = 8**
Treatment algorithm	**Bilateral anterior CS (+BTA)**	**Bilateral anterior CS + BTA (+ PPP)**	**Bilateral anterior CS + BTA + PPP**
Age, years, median (range)	67 (46-74)	68 (63-77)	63 (28-69)
BMI, kg/m² (range)	31.4 (24.7-43.0)	29.8 (22.7-36.8)	36.3 (25.5-43.3)
Recurrent hernia (%)	5 (55.6)	3 (50.0)	6 (75.0)
EHS classification			
M1-M4W3	1 (11.1)	2 (33.3)	2 (25.0)
M1-M5W3	0 (0)	2 (33.3)	1 (12.5)
M2-M4L2W3	1 (11.1)	0 (0)	0 (0)
M2-M5W3	0 (0)	1 (16.7)	4 (50.0)
M2-M5W2	1 (11.1)	0 (0)	0 (0)
M2-M5L2W3	0 (0)	0 (0)	1 (12.5)
M3-M4W3	1 (11.1)	0 (0)	0 (0)
M3-M5W3	4 (44.4)	0 (0)	0 (0)
L2-W3	1 (11.1)	0 (0)	0 (0)
Missing	0 (0)	1 (16.7)	0 (0)
BTA only (%)	3 (33.3)	2 (33.3)	1 (12.5)
PPP only (%)	1 (11.1)	0 (0)	2 (25.0)
PPP + BTA (%)	5 (55.6)	4 (66.7)	5 (62.5)
Surgery (%)	9 (100.0)	5 (83.3)	8 (100.0)
Surgery time, minutes (range)	265 (150-399)	260 (220-370)	323 (215-396)
Type of surgery			
Anterior CS, bilateral (%)	2 (22.2)	5 (83.3)	8 (100.0)
TAR, bilateral (%)	1 (11.1)	0 (0)	0 (0)
Anterior CS, unilateral (%)	1 (11.1)	0 (0)	0 (0)
TAR, unilateral (%)	1 (11.1)	0 (0)	0 (0)
Comb. anterior CS and TAR (contralateral sides) (%)	3 (33.3)	0 (0)	0 (0)
No CS (%)	1 (11.1)	0 (0)	0 (0)
No repair (%)	0 (0)	1 (16.7)	0 (0)
Mesh location			
Intraperitoneal	4 (44.4)	5 (83.3)	8 (100.0)
Retromuscular	5 (55.6)	0 (0)	0 (0)
Mesh type			
Synthetic	9 (100)	5 (83.3)	7 (87.5)
Biologic	0 (0)	0 (0)	1 (12.5)

Table 3. Surgical characteristics per subgroup from the algorithm

BMI: Body Mass Index, EHS: European Hernia Society, BTA: botulinum Toxin A, PPP: progressive preoperative pneumoperitoneum, CS: component separation, TAR: transverse abdominal release, Comb.: combination

Intra- and postoperative complications

With regard to the primary outcome, in four patients (18.1%), the anterior fascia could not be closed during the initial operation. One patient had a small bowel perforation during adhesiolysis, which was repaired immediately during the first operation, but a second stage repair a few days later was required. In three other patients (13.6%) the anterior layer could only be closed using a small part of the hernia sac to cover the intraperitoneal mesh. With regard to the secondary endpoints, 16 patients (72.7%) developed 23 surgical site occurrences (SSOs) postoperatively (summarized in Table 4). Twelve patients (54.5%) had a surgical site infection (SSI), of which six patients (26.1%) had a deep infection. One deep infection was managed by antibiotic treatment alone, two deep infections required (partly) surgical mesh removal, and the remaining three were treated with negative pressure therapy. Other SSOs included seromas (N=4, 18.2%), hematomas (N=4, 18.2%), postoperative fascia dehiscence (N=3, 13.6%). None of these SSOs required additional therapy, except for one seroma, which was drained by ultrasound guidance and subsequently drained during surgery. No postoperative enterocutaneous fistulas were seen. Other complications included pneumonias in three patients, of whom two needed admission to the intensive care unit. A total of three patients (13.6%) experienced a hernia recurrence, of which one received surgical repair. Hernia recurrence repair was performed and a synthetic mesh was placed intraperitoneally. Cumulatively, five surgical interventions took place: one for hernia recurrence and a deep SSI (4.5%) and four (18.2%) for other postoperative complications.

Hernia width	**Width 14-18 cm** **N = 9**	**Width 18-22 cm** **N = 5***	**Width >22 cm** **N = 8**
Treatment algorithm	**Bilateral anterior CS (+BTA)**	**Bilateral anterior CS + BTA (+ PPP)**	**Bilateral anterior CS + BTA + PPP**
Direct fascial closure achieved (%)	9 (100)	4 (80.0)	5 (62.5)
Recurrence (%)	0 (0)	1 (20.0)	2 (25.0)
Reoperation for either recurrence or complication (%)	0 (0)	2 (40.0)	3 (37.5)
Patients with ≥ 1 SSO	5 (55.5)	3 (60.0)	8 (100.0)
Total SSO	7	4	13
Surgical site infection (%)	4 (44.4)	3 (60.0)	6 (75.0)
	4 (44.4)	1 (20.0)	2 (25.0)
Superficial or wound	0 (0)	2 (40.0)	4 (50.0)
dehiscence	1 (11.1)	0 (0)	3 (37.5)
Deep	2 (22.2)	0 (0)	2 (25.0)
Seroma (%)	0 (0)	1 (20.0)	2 (25.0)
Hematoma (%)	0 (0)	0 (0)	0 (0)
Fascia dehiscence (%)			
Enterocutaneous fistula formation (%)			
Follow-up, months (median, range)	17 (10-40)	13 (12-31)	32.5 (19-60)

Table 4. Recurrences and Surgical Site Occurrences (SSOs) per subgroup from the algorithm.

* 5 as one patient did not receive repair.

Discussion

Preoperative preparation of patients with giant ventral and incisional hernias is essential to obtain the best possible outcomes in terms of fascial closure rate. However, the effects of preoperative aids cannot be enhanced intraoperatively; the needed effect size has to be determined beforehand. Therefore, a standardized preoperative strategy based on clinical and radiological parameters would be useful to estimate the needed effect size, informing on whether there is need for the use of BTA, PPP, or both. This cohort of 23 patients, treated according to a standardized algorithm for a giant ventral hernia with or without LOD, shows that BTA and PPP facilitate closure in ventral hernia repair. The primary fascial closure rate is 82%.

Component separation technique

Component separation techniques were used as the first tool in our algorithm to facilitate medialization of the rectus muscles and closure of the anterior fascia. Surgeons that refrain from using component separation techniques might not achieve anterior fascial closure in all patients, as illustrated by Renard et al. (primary closure in 42 out of 45 patients, 94%) [7]. In our study, anterior CST and TAR were applied in all but one patient; anterior CST was planned in addition to BTA for this patient, but BTA alone made anterior fascial closure possible. Despite being associated with more wound complications than TAR [22], anterior CST renders nearly 6 cm of medialization of the rectus sheath (in postmortem human specimens), which can contribute to tension-free fascial closure [6]. In three patients in our study, to avoid intraperitoneal mesh placement and obtain anterior fascia closure, a unilateral TAR was done on one side to facilitate the closure of the posterior layer, and a unilateral anterior CST was done on the other side to ensure anterior fascial closure. In none of the patients both anterior CST and TAR were performed at the same side. Another component separation method could be represented by the endoscopic external oblique release as described by Rosen et al. [23], but as the achieved fascial advancement is limited to approximately 80% of what can be achieved by an open technique, the latter was used in our study.

BTA

If anterior CST was estimated not to be enough for achieving anterior closure of the fascia, BTA was applied 4–6 weeks preoperatively. Only two protocols for BTA injections have so far been described: a three-point and five-point technique, respectively [20, 24]. Either one of these does not seem preferable over the other. BTA alone has been reported to give a 0.5–1.5 cm extra muscle length on each side of the abdominal wall on average. Other authors, however, found 1–5 cm of myofascial advancement with the use of BTA [12, 13, 25-27]. In this study, the addition of BTA injections resulted in an extra increase in length of 2.0–3.0 cm of the lateral abdominal wall muscles, without causing additional complications. This finding is in line with the current literature; no complications of BTA use as a preoperative aid have been recorded, only minor inconveniences such as bruising after injection or a sensation of bloating [12]. One study even found an additional analgesic effect postoperatively of BTA [28].

PPP

In case a significant loss of domain of more than 20% was calculated preoperatively, the use of PPP was indicated, as shown in our algorithm (Fig. 1). PPP insufflations were performed daily with ambient air, until the patient experienced scapular pain, abdominal pain, or dyspnoea. The use of ambient air has been advocated, because nitrous oxide, carbon dioxide, and oxygen are absorbed four times faster in the peritoneal space than ambient air [10, 29]. This causes the necessity to top up the volume often and with large quantities, while the use of ambient air results in easier maintenance of the pneumoperitoneum. No current consensus has been reached with regard to the amount of air to be injected, the frequency of the insufflations, and the length of the period the pneumoperitoneum should be maintained. Therefore, we used 2 L at the time of catheter placement intra-operatively and 1 L daily. It is suggested that PPP does not cause further benefit after 6–10 days [29]. However, CT scans at 7 days after starting PPP showed only partial reduction of the hernia content in most of our patients, with limited air accumulation in the abdominal cavity itself. Therefore, we continued PPP for a maximum of 21 days. The average LOD was 53% before admission

(median 29%). PPP caused a mean increase in HSV/ACV ratio of 4%. This increase is understandable from the law of Laplace, and was also found by Sabbagh et al. [8] reporting a 1%-increase in the ratio incisional hernia volume to total peritoneal content. Other authors, however, report a significant decrease in this ratio, from 5 to 22% [7, 15, 30]. Their findings could justify the use of an abdominal binder between PPP sessions, to restrict air going to the hernia sac. However, air inside the hernia can cause lysis of possible adhesions and facilitate fascial closure [31]. Complications related to PPP in our study are predominantly hematomas, and one patient died because of an extensive bleeding and hemodynamic shock (however, probably also related to his frail preoperative state). We treated all our patients with a therapeutic dosage of low molecular weight heparins from the start of PPP to prevent pulmonary embolisms. This serious complication has been described using laparoscopy [32] and is probably caused by increasing pressure at the level of the caval vein. However, in the light of our current findings—showing a high incidence of hematomas and bleeding complications—it might be better to use prophylactic dosage LMWH during PPP. Other authors describe subcutaneous emphysema, shoulder pain, abdominal pain, nausea, anxiety, intestinal perforation, and even mortality [7, 10, 15, 29, 31, 33]. Therefore, PPP asks for deliberate use in specific patient groups only. An evidence-based cut-off for LOD should be established to help surgeons decide on when to use PPP as a preoperative aid for hernia repair. As the primary goal is to close the anterior fascia, lenient cut-off for LOD should be utilized.

Complications

Surgical repair of these giant hernia defects was accompanied by several complications. Twelve patients (54.5%) experienced a surgical site infection (superficial or deep) and 3 patients (13.6%) had a recurrence. Five patients (22.7%) had to have a reoperation for either a recurrence or postoperative complication. These complications could not have entirely been avoided, as this is a very complex patient group. More than 90% of the patients were overweight (BMI>25 kg/m2) and many had comorbidities (as shown in Table 1). When compared to the literature on ventral hernias with LOD, our SSI rate of 54.5% seems high. This might be partially be explained by the fact

that we included wound dehiscence without proof of positive cultures in the superficial SSI rate. Other authors describe infection rates between 5 and 26% [7, 19, 34-38]. Also, the number of patients receiving a reoperation seems relatively high with 22.7%, compared to a 10–15% reoperation rate [35, 38]. A possible explanation might be that we considered negative pressure wound therapy, as initiated with wound debridement in the OR, as a reoperation. Only one other study—more in line with our data—finds that one-third of the patients had to be reoperated [36]. These relatively high numbers could be due to the rather extreme width of the hernias researched in this study. Patient selection may have differed from the abovementioned studies. Additionally, the large number of comorbidities present in the researched group hinders the direct comparison of outcomes with findings from other authors. The number of patients having a recurrence (13.6%) is within line of expectations for these complicated hernias. Other authors report 4–16% recurrences [7, 19, 34-38].

Limitations

This is a retrospective cohort study, which is sensitive to bias. Also, only 23 patients were analyzed. The results must, therefore, be interpreted with caution, as these numbers are insufficient to provide sound statistical comparisons. Additionally, some patients had a relatively short follow-up period, and CT scans were not always available to confirm that indication for PPP (as through our algorithm) was indeed present; these both are the drawbacks of the presented study. However, LOD is most of the time obvious at clinical examination, so bias on this point would be relatively low. Despite these limitations, the data of these patients add to the current body of knowledge about the combined use of BTA and PPP, what it can offer in hernia defect closure and the potential risks.

Implications

The combination of anterior CST and BTA seems safe and effective, leading to an anterior fascial closure rate of 82% in our study. PPP use might require more critical deliberation whether it is worth the risk as it resulted in a high complication rate of 29%. The standardized treatment algorithm prevented the surgeon from facing unforeseen intraoperative difficulties in closing

the anterior fascia. However, the issue we came across during the usage of proposed algorithm in clinical practice is that it cannot always be successfully applied, as it is not a validated instrument. LOD was only measured when the estimated hernia width was > 18 cm, but had implications for the preoperative treatment, while LOD can also be present in hernias of less than 18 cm width. Meaning, undertreatment might have taken place: patients with LOD, but with an estimated effect width of < 18 cm, could possibly also have benefited from the additional PPP treatment.

On the other hand, overtreatment might also have been present, as the exact benefits and limitations of BTA treatment remain unclear; in some patients, fascial closure might have been achieved without the use of BTA or PPP. Using BTA is expensive and, as BTA is not reimbursed by the insurance companies in Belgium, it poses an additional cost of approximately 500–600 euros for the patient.

PPP is described to cause a decrease in the LOD of the hernia, facilitating tension-free closure of the fascia during repair. An additional advantage of PPP is the lysis of adhesions caused by the insufflated air [31]. A drawback of PPP is that it is even more expensive, as it required preoperative hospital stay in our study. As reported by Renard et al. [7], admission is not mandatory, but safety was considered of utmost importance in our study (as was observed with the patient suffering an AV-block during insufflation). Moreover, PPP showed a high complication rate of 29% which included severe complications, PPP can cause pain, and PPP is generally experienced as unpleasant by patients, possibly resulting in a lower quality of life. An evidence-based protocol might be of help with indications for its use, and with regard to the amount of air to be insufflated and the number of days the pneumoperitoneum should be maintained. However, as it involves a very heterogeneous and relatively small group of patients with many variables influencing the final outcome, this might be elusive. The individual value of BTA, PPP, and CST cannot be determined based on the results from this study, nor has their value been elucidated in other studies, which only suggest optimistic results of the combined use of these methods [35]. The value of a specific preoperative aid is difficult to determine as the number of patients treated in the current study is too small and overtreatment might have taken place to be certain to

achieve fascial closure. Because BTA is associated with fewer complications, it would be useful to distinguish between patients with a hernia with LOD that could be treated with BTA alone, CST alone, and patients that would need the combination of BTA and PPP, and possibly additional CST. This analysis clearly demonstrates, however, that a standardized algorithm may be considered as a guidance during the pre- and intra-operative surgical decision-making, but both preoperative CT assessment and clinical examination remain mandatory to determine the best approach for each individual patient. Larger studies and pooling of data would be required to give recommendations with regard to optimal selection of preoperative preparation methods.

Conclusions

This study is a description of 23 patients with complex ventral hernia repair facilitated by Botulinum toxin A and preoperative progressive pneumoperitoneum. BTA seems safe to aid closure, whereas PPP requires critical consideration for its use. Further research should be conducted to determine both indications and outcome parameters for each of these preoperative tools in abdominal wall reconstruction.

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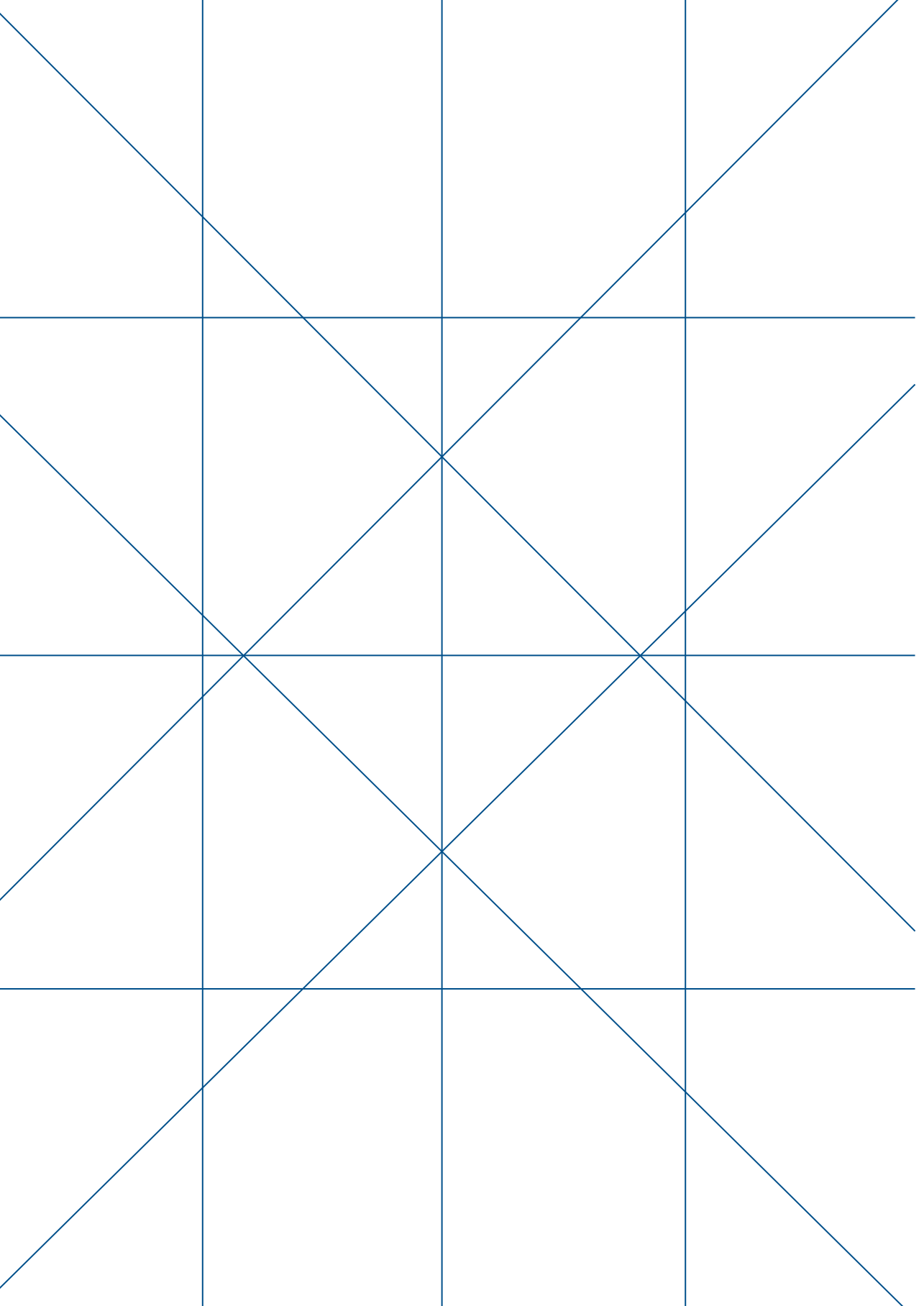

Chapter 9

Functional outcomes in symptomatic versus asymptomatic patients undergoing incisional hernia repair: do we replace one problem with another? A prospective cohort study in 1,312 patients

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Abstract

Background

Incisional hernias can be associated with pain or discomfort. Surgical repair especially mesh reinforcement, may likewise induce pain. The primary objective was to assess the incidence of pain after hernia repair in patients with and without pre-operative pain or discomfort. The secondary objectives were to determine the preferred mesh type, mesh location and surgical technique in minimizing postoperative pain or discomfort.

Materials and methods

A registry-based prospective cohort study was performed, including patients undergoing incisional hernia repair between September 2011 and May 2019. Patients with a minimum follow-up of 3-6 months were included. The incidence of hernia related pain and discomfort was recorded pre- and postoperatively.

Results

A total of 1312 patients were included. Pre-operatively, 1091 (83%) patients reported pain or discomfort. After hernia repair, 961 (73%) patients did not report pain or discomfort (mean follow-up=11.1 months). Of the pre-operative asymptomatic patients (n=221), 44 (20%, moderate or severe pain: n=14, 32%) reported pain or discomfort after mean follow-up of 10.5 months. Of those patients initially reporting pain or discomfort (n=1091), 307 (28%, moderate or severe pain: n=80, 26%) still reported pain or discomfort after a mean follow-up of 11.3 months postoperatively.

Conclusion

In symptomatic incisional hernia patients, hernia related complaints may be resolved in the majority of cases undergoing surgical repair. In asymptomatic incisional hernia patients, pain or discomfort may be induced in a considerable number of patients due to surgical repair and one should be aware if this postoperative complication.

Introduction

Incisional hernia is a common complication after abdominal surgery with incidence rates of more than 30% in high-risk patients, such as patients with abdominal aortic aneurysms and obese patients [1-4]. Incisional hernias may cause discomfort, pain, and an impaired quality of life [5]. Nowadays, mesh reinforcement is the preferred treatment for incisional hernia repair and for prevention in patients with a high risk for developing an incisional hernia [6, 7]. However, mesh reinforcement has also been associated with chronic pain [8]. Moreover, among patients there is an increased resistance for the use of surgical meshes in general, due to negative reports in media (including social media). Is this negative view of the media on incisional hernia repair causing postoperative chronic pain justified? And, do we replace incisional hernia related pain with pain caused by hernia repair?

Several previous studies reported on the long-term incidence of pain or discomfort after primary and incisional hernia repair, reported incidences varying widely from 3% to over 61% [9-12]. These differences are likely explained by multiple factors, such as differences in assessment and different surgical techniques [12-14]. Additionally, pain is usually assessed as secondary outcome in studies with varying objectives. Therefore, the patient population may vary greatly in comparison to the general population of patients presenting with an incisional hernia.

Incisional hernia research mostly emphasizes on reducing recurrence rates, usually in relation to different mesh types and different surgical approaches. However, in contrast to inguinal hernia, the functional outcomes of patients who underwent incisional hernia repair are studied less frequently. Nevertheless, both outcomes are equally important to the individual and may aide in clinical decision-making, functional outcomes especially being of importance to patients with smaller incisional hernias who are either asymptomatic or have only minor complaints.

The primary objective of this registry-based study, was to assess the incidence of pain after incisional hernia repair in patients with and without pre-operative pain or discomfort.

Material and methods

This prospective cohort study was performed within the French Hernia-Club registry. The French Hernia-Club registry is approved by the French 'Commission Nationale de l'Informatique et des Libertés' (CNIL registration number: 1993959v0) and complies to the General Data Protection Regulation. Because this study is registry-based and guarantees completely anonymized data, additional participant consent and approval were not required according to the French and Dutch national ethical standards. This study was conducted following the STROBE (Strengthening the Reporting of Observational studies in Epidemiology), STROCSS (Strengthening the Reporting of Cohort Studies in Surgery) statements, and the European Registry of Abdominal Wall Hernias (EuraHS) recommendations [15-17].

Study design

A registry-based, prospective cohort study was performed. Adult patients undergoing incisional hernia repair registered in the French Hernia-Club registry, between September 1, 2011 and May 22, 2019 were eligible for inclusion. For this study, patients were selected with a minimum follow-up of 3-6 months with available data on pre- and postoperative pain and discomfort. Two groups were defined:

- Patients without pre-operative discomfort or pain: asymptomatic patients.
- Patients with pre-operative discomfort or pain: symptomatic patients.

Patients were considered symptomatic if they experienced either pain, sensitive complaints (dysesthesia, hypoesthesia), incarceration of the bowel, or discomfort not otherwise specified. At the end of follow-up, the incidence of postoperative pain or discomfort was compared in these groups.

Hernia-Club registry

The Hernia-Club registry is a collaborative, prospective, anonymized online database of all surgical procedures for primary and incisional hernias. French surgeons specialized in abdominal wall surgery performed all surgical procedures. Each participating surgeon must accept and sign the Charter

of Quality, which states that: 'all input must be registered in a consecutive, unselected and exhaustive manner and in real time.' A total of 191 parameters were collected by the operating surgeon and the blinded, independent, clinical research associates, using online forms. Parameters comprise data from screening, pre-, peri-, and postoperative periods. Participants consent to random peer review of original medical charts to ensure high-quality data. The medical records were also checked in the case of any discrepancies. All collected parameters in this database were fully compatible with the EuraHS international online platform, as well as the European Hernia Society (EHS) classification incisional abdominal wall hernias [17, 18].

Data collection

Baseline patient characteristics extracted from the registry comprised age, sex, body mass index (BMI), smoking, diabetes mellitus, recent corticosteroid use, recent radiotherapy, recent chemotherapy, history of abdominal aortic aneurysm (AAA), connective tissue disorder, anticoagulant use or coagulopathy, history of ventral hernia, family history of hernia, American Society of Anesthesiologists (ASA) classification, presence of ascites, chronic cough, constipation and heavy lifting. With reference to pre-operative symptoms, the presence of pain, sensitive complaints (dysesthesia, hyperesthesia, hyperpathia, hypoesthesia) or other (non-specified) discomfort were extracted.

Baseline hernia characteristics comprised presence of recurrent hernia, previous surgery with mesh, location of previous mesh (onlay, inlay, retromuscular sublay, preperitoneal sublay, intraperitoneal onlay), defect location in the midline (subxiphoid, epigastric, peri-umbilical, infra-umbilical, suprapubic), if applicable lateral defect location lateral (subcostal, flank, iliac, lumbar) and width of the defect according to EHS width classification [18].

Surgical characteristics comprised of emergency procedure, incarceration, open or laparoscopic procedure, mesh position (onlay, inlay, retromuscular sublay, preperitoneal sublay, intraperitoneal, component separation, no mesh/suture closure), mesh fixation (suture, tacker/stapler, self-adhesive mesh), duration of surgery, Altemeier wound classification [19] and antibiotic treatment.

Outcomes

The primary outcome was the incidence of pain or discomfort after hernia repair. Pain was assessed at the outpatient clinic at two time points, between 3 and 6 months postoperatively and approximately 12 months postoperatively. If repeated measurements were present the last observation available was carried forward. If patients were willing to participate, a long-term follow-up questionnaire was performed after approximately two years. Patients received the questionnaire by telephone which was performed by an independent clinical research associate who was blinded for the used technique.

In this questionnaire, symptoms were specified with use of the 4 scales Verbal Rating Scale (VRS) (no pain, mild pain/discomfort moderate pain, severe pain), presence of a sensitive scar, less sensitivity of the skin and other discomfort. Additionally, the presence of bulging, sensation of non-solid scar, the frequency of discomfort (rarely, weekly, daily), and functional limitations due to discomfort (no limitations, some limitations, severe limitations of general activities) were assessed.

Statistical analysis

Statistical analysis was performed with SPSS version 25 (IBM SPSS Statistics for Windows, version 25.0.0.1, IBM Corp, Armonk, New York). Continuous variables are presented as mean and standard deviation (SD). Discrete variables are presented as absolute numbers and percentages. Continuous variables were compared with a Student's T-test or Mann Whitney U test, as appropriate. Discrete variables were compared with a chi-quare test. The primary outcome, the incidence of pain and discomfort postoperatively, was compared between the pre-operatively asymptomatic and symptomatic patients, was reported as absolute numbers and percentages. Additionally, these proportions were compared with a X^2 test.

Secondarily, to assess factors potentially associated with long-term postoperative pain and discomfort, uni- and multivariable logistic regression was used. For univariable logistic regression a complete case analysis was performed, including all variables of interest. To ensure maximized use of available data, multiple imputations were performed to compensate for missing

data (0-8.3%), in advance of multivariable logistic regression. Multiple imputations were performed with ten imputations. Variables potentially associated with pain or discomfort after univariable analysis ($p<0.2$) and variables of clinical interest were considered for multivariable analysis. Backward elimination was used to reduce the model. The saturated model was compared to the reduced model with likelihood ratio chi-square test. Variables with a strong mutual correlation were not fitted simultaneously. To prevent overfitting a maximum of one variable was fitted for each ten events. Age appeared not linearly associated to the outcome, therefore age was fitted in 4 quartiles. Glue (n=8) fixation and inlay mesh (n=5) placement were rarely applied, therefore these cases were excluded from multivariable analysis. The R^2-value was used to assess the overall variance that could be predicted. A p-value of <0.05 was considered statistically significant.

Results

A total of 1312 included patients underwent surgery for incisional hernia repair (Figure 1). Pre-operatively, 1091 (83%) patients reported pain or discomfort (symptomatic patients). A total of 221 (17%) patients reported no pre-operative pain or discomfort (asymptomatic patients).

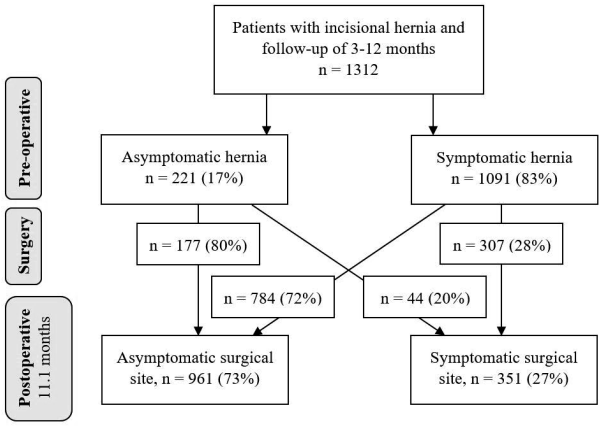

Figure 1. Flowchart representing initially asymptomatic and symptomatic patients undergoing hernia repair.

Patient baseline characteristics

All baseline patient characteristics are presented in Table 1. Patients who presented with a symptomatic incisional hernia were more likely to be female and had a slightly higher BMI, compared to asymptomatic patients (sex, male/female: 60.2/39.8% asymptomatic *versus* 45.2/54.8% symptomatic, $p<0.001$; BMI: 27.9 kg/m^2 asymptomatic *versus* 29.5 kg/m^2 symptomatic, $p<0.001$). Additionally, those patients who presented with a symptomatic incisional hernia more often had a recurrent hernia (31.1% asymptomatic *versus* 40.1% symptomatic, $p=0.012$). Factors related to an increased intra-abdominal pressure such as chronic cough and constipation were more frequently reported by symptomatic patients, compared to asymptomatic patients (chronic cough: 7.9% asymptomatic *versus* 15.3% symptomatic, $p<0.001$; constipation: 4.2% asymptomatic *versus* 7.8% symptomatic, $p=0.06$).

	Overall patients	Asymptomatic	Symptomatic	P	N missing
N	1312	221	1091		
Age (years)	65 SD 13.6	65.8 SD 13.5	64.9 SD 13.6	0.369	3
Sex					0
Male	626 (47.7)	133 (60.2)	493 (45.2)	**< 0.001**	
Female	686 (52.3)	88 (39.8)	598 (54.8)	**< 0.001**	
BMI (kg/m²)	29.2 SD 6.2	27.9 SD 6.1	29.5 SD 6.1	**< 0.001**	24
Current smoking	215 (17.7)	31 (15.6)	184 (18.1)	0.39	97
Diabetes mellitus	224 (17.3)	36 (16.4)	188 (17.5)	0.69	17
Corticosteroids	52 (4)	8 (3.6)	44 (4.1)	0.75	17
Radiotherapy	28 (2.2)	8 (3.6)	20 (1.9)	0.10	17
Chemotherapy	138 (10.7)	24 (10.9)	114 (10.6)	0.89	17
History of AAA	9 (0.7)	2 (0.9)	7 (0.6)	0.66	7
Connective tissue disorder	2 (0.2)	0 (0)	2 (0.2)	0.53	7
Anticoagulant use or coagulopathy	207 (16)	34 (15.5)	173 (16.1)	0.81	17
History of ventral hernia	503 (38.5)	68 (31.1)	435 (40.1)	**0.01**	7
Family history of hernia	11 (0.8)	3 (1.4)	8 (0.7)	0.35	7
ASA classification					9
I-II	952 (73.1)	167 (75.6)	785 (72.6)	0.36	
III-IV	351 (26.9)	54 (24.4)	297 (27.4)	0.36	
Ascites	5 (0.4)	0 (0)	5 (0.5)	0.32	18
Chronic cough	182 (14.1)	17 (7.9)	165 (15.3)	**< 0.001**	18
Constipation	93 (7.2)	9 (4.2)	84 (7.8)	0.06	18
Heavy lifting	90 (7)	11 (5.1)	79 (7.3)	0.24	18

Table 1. Patient baseline characteristics for asymptomatic and symptomatic patients with an incisional hernia.

BMI: body mass index; AAA abdominal aortic aneurysm; ASA American Society of Anesthesiologists. Continuous variables are presented a mean and SD, discrete variables are presented as absolute number and (percentage). P for student T-test, fishers exact test or X^2test as appropriate.

Hernia characteristics

Hernia characteristics are presented in Table 2. Patients who presented with a symptomatic incisional hernia and who had received mesh surgery, slightly more often had received an intraperitoneal mesh (9.5% asymptomatic *versus* 16.7% symptomatic, p=0.01). The proportion of patients who presented with a symptomatic hernia and who had received mesh surgery was equal for all other mesh locations, compared to the asymptomatic patients. With reference to hernia location the distribution of patients who presented with a symptomatic or asymptomatic incisional hernia appeared relatively equal. Slightly more symptomatic patients presented with a suprapubic hernia and slightly less with a epigastric hernia, compared to asymptomatic patients (suprapubic hernia: 3.8% asymptomatic *versus* 8.9% symptomatic, p=0.01; epigastric hernia: 20.8% asymptomatic *versus* 14% symptomatic, p=0.01). Of those patients who had a lateral hernia, patients with a subcostal lateral hernia more often reported pain or discomfort and patients with a iliac lateral hernia less often reported pain or discomfort at baseline (subcostal hernia: 2.8% asymptomatic *versus* 6.2% symptomatic, p=0.05; iliac hernia: 15.7% asymptomatic *versus* 10.7% symptomatic, p=0.03). With reference to the EHS width classification, slightly more symptomatic patients presented with a grade W3 hernia (≥10 centimeters), and slightly less with a grade W1 hernia (<4 centimeters), compared to asymptomatic patients (W1 hernia: 54.9% asymptomatic *versus* 43.8% symptomatic, p=0.004; W3 hernia: 9.3% asymptomatic *versus* 15.8% symptomatic, p=0.02).

	Overall patients	Asymptomatic	Symptomatic	P	N missing
N	1312	221	1091		
Recurrent hernia	318 (24.8)	41 (19)	277 (26)	**0.03**	29
Previous surgery with mesh*					14
No mesh	867 (66.8)	159 (71.9)	708 (65.7)	0.07	
Prefascial (onlay)	19 (1.5)	3 (1.4)	16 (1.5)	0.89	
At the bangs (inlay)	13 (1)	3 (1.4)	10 (0.9)	0.56	
Retromuscular (sublay)	120 (9.2)	19 (8.6)	101 (9.4)	0.72	
Preperitoneal (sublay)	58 (4.5)	10 (4.5)	48 (4.5)	0.96	
Intraperitoneal (onlay)	201 (15.5)	21 (9.5)	180 (16.7)	**0.01**	
Not specified	20 (1.5)	6 (2.7)	14 (1.3)	0.12	
Defect location midline					17
Subxiphoid	46 (3.6)	7 (3.2)	39 (3.6)	0.79	
Epigastric	196 (15.1)	45 (20.8)	151 (14)	**0.01**	
Peri-umbilical	474 (36.6)	88 (40.7)	386 (35.8)	0.17	
Infra-umbilical	239 (18.5)	31 (14.4)	208 (19.3)	0.09	
Suprapubic	104 (8)	8 (3.7)	96 (8.9)	**0.01**	
Only lateral location	236 (18.2)	37 (17.1)	199 (18.4)	0.65	
Defect location lateral					17
Subcostal	73 (5.6)	6 (2.8)	67 (6.2)	**0.05**	
Flank	77 (5.9)	8 (3.7)	69 (6.4)	0.13	
Iliac	149 (11.5)	34 (15.7)	115 (10.7)	**0.03**	
Lumbar	18 (1.4)	0 (0)	18 (1.7)	0.06	
Only medial	978 (75.5)	168 (77.8)	810 (75.1)	0.40	
EHS width classification					51
W1: < 4 cm	575 (45.6)	112 (54.9)	463 (43.8)	**0.004**	
W2: ≥ 4-10 cm	500 (39.7)	73 (35.8)	427 (40.4)	0.22	
W3: > 10 cm	186 (14.8)	19 (9.3)	167 (15.8)	**0.02**	

Table 2. Hernia characteristics for asymptomatic and symptomatic patients with an incisional hernia.

*EHS: European Hernia Society. Continuous variables are presented a mean and SD, discrete variables are presented as absolute number and (percentage). P for student T-test, fishers exact test or X^2test as appropriate. * Not directly a recurrent hernia.*

Surgical characteristics

Surgical characteristics are presented in Table 3. Almost all patients who received an emergency procedure were symptomatic incisional hernia patients. By definition, patients with a non-reducible incarceration were considered symptomatic, this occurred in 30 (2.3%) patients. In general, different surgical treatments, were evenly distributed among symptomatic and asymptomatic patients. In symptomatic patients undergoing mesh repair, suture fixation appeared to be used slightly more often, compared to asymptomatic patients (54% asymptomatic *versus* 65.6% symptomatic, p=0.002).

	Overall patients	Asymptomatic	Symptomatic	P	N missing
N	1312	221	1091		
Emergency procedure	55 (4.2)	2 (0.9)	53 (4.9)	**0.01**	8
Incarceration	30 (2.3)	0 (0)	30 (2.8)	**0.01**	10
Open procedure	1134 (87.4)	190 (87.2)	944 (87.5)	0.89	15
Laparoscopic procedure	163 (12.6)	28 (12.8)	135 (12.5)	0.89	15
Mesh position					19
Prefascial onlay	33 (2.6)	2 (0.9)	31 (2.9)	0.10	
Sublay (retro-muscular/ pre-peritoneal)	596 (46.1)	113 (52.1)	483 (44.9)	**0.05**	
Intraperitoneal onlay	548 (42.4)	81 (37.3)	467 (43.4)	0.09	
No mesh	110 (8.5)	21 (9.7)	89 (8.3)	0.5	
Mesh fixation					134
Suture	749 (63.6)	109 (54)	640 (65.6)	**0.002**	
Tacker/stapler	278 (23.6)	55 (27.2)	223 (22.8)	0.18	
Self-adhesive	59 (5)	13 (6.4)	46 (4.7)	0.30	
No mesh	110 (9.3)	21 (10.4)	89 (9.2)	0.57	
Duration of surgery, min	94 SD 60	102 SD 77	93SD 55	0.09	49
Altemeier wound classification					7
Clean	1161 (89)	188 (85.8)	973 (89.6)	0.11	
Clean contaminated	91 (7)	17 (7.8)	74 (6.8)	0.62	
Contaminated	37 (2.8)	12 (5.5)	25 (2.3)	**0.01**	
Dirty	16 (1.2)	2 (0.9)	14 (1.3)	0.64	
Antibiotic treatment					15
None	140 (10.8)	39 (18.1)	101 (9.3)	**<0.001**	
Prophylactic	1023 (78.9)	166 (76.9)	857 (79.3)	0.43	
Therapeutic	134 (10.3)	11 (5.1)	123 (11.4)	**0.01**	

Table 3. Surgical characteristics for asymptomatic and symptomatic patients with an incisional hernia.

IPOM: Intraperitoneal Onlay Mesh. Continuous variables are presented a mean and SD, discrete variables are presented as absolute number and (percentage). P for student T-test, fishers exact test or X^2test as appropriate.

Long-term postoperative pain and discomfort

The incidence of postoperative pain in relation to pre-operative symptoms is graphically summarized in Figure 1. Detailed data on long-term postoperative pain and discomfort are presented in Table 4. Data on postoperative pain and discomfort was recorded after a mean of 11.1 ± 4.5 months. In initially asymptomatic patients who had received hernia repair surgery, 44 patients (20%, total n=221) reported pain or discomfort after a mean of 10.5 ± 4.0 months. In initially symptomatic patients who had received hernia repair surgery 961 patients, (72%, total n=1091) reported no pain or discomfort after a mean of 11.3 ± 4.5 months. When considering the severity of postoperative symptoms, the majority of patients reported only minor complaints. Mild pain was reported by 22 out of 44 patients (50%) of initially asymptomatic patients and by 160 out of 307 patients (52%) of initially symptomatic patients. Moderate pain or severe pain was reported in 14 out of 44 patients (30%) of initially asymptomatic patients and in 80 out of 307 (26%) of initially symptomatic patients. Only sensitive complaints (dysesthesia, hyperesthesia, hyperpathia or hypoesthesia) were reported in a minority of patients with postoperative pain or discomfort 30 out of 351 patients (8.5%).

	Overall patients	**Asymptomatic**	**Symptomatic**	**P**	**N missing**
N	1312	221	1091		
Follow-up (months)	11.1 SD 4.5	10.5 SD 4.0	11.3 SD 4.5	**0.016**	62
Any discomfort	351 (26.8)	44 (19.9)	307 (28.1)	**0.01**	0
Discomfort specified				**0.05**	
Sensitive scar only	32 (2.4)	4 (1.8)	28 (2.6)		
VRS mild pain/ discomfort	182 (13.9)	22 (10)	160 (14.7)		
VRS moderate pain	78 (5.9)	12 (5.4)	66 (6)		
VRS severe pain	16 (1.2)	2 (0.9)	14 (1.3)		
Less sensitivity only	30 (2.3)	1 (0.5)	29 (2.7)		
Other discomfort	13 (1)	3 (1.4)	10 (0.9)		

Table 4. Discomfort between 3 and 12 months after surgery.

VRS: Verbal Rating Scale; Continuous variables are presented a mean and SD, discrete variables are presented as absolute number and (percentage). P for student T-test, fishers exact test or X^2test as appropriate.

Long-term follow-up questionnaire

A total of 814 patients completed a follow-up questionnaire by telephone or by mail after a mean follow-up of 24.7 ± 11.4 months. Results of this questionnaire are summarized in Table 5. Overall, the incidence of patients experiencing any postoperative complaints including pain or discomfort was lower as compared to 12 months follow-up. 196 out of 841 patients (23.7%) of patients who returned the questionnaire experienced any complaints. Only 144 patients (17.1%) experienced pain or discomfort. Of those patients experiencing pain or discomfort, the initially symptomatic patients (n=706) appeared to experience more severe symptoms, as compared to the initially asymptomatic (n=135) patients (discomfort: 9.2% asymptomatic *versus* 18.7% symptomatic, p=0.01). The initially asymptomatic patients who experienced pain or discomfort (n=12), reported mild pain in 66.7% of cases. In comparison, those patients who were initially symptomatic and who were still experiencing pain or discomfort (n=132), reported moderate pain in 25.8% of cases, and severe pain in 11.4% of cases. Additionally, those patients who were initially symptomatic reported more limitations in daily life due to their symptoms, this was only rarely reported in the initially symptomatic patients who experienced pain or discomfort (Table 5).

	Overall patients	Asymptomatic	Symptomatic	P	N missing
N	841	135	706		
Written questionnaire	484 (57.6)	91 (67.4)	393 (55.7)	**0.01**	0
Phone questionnaire	357 (42.4)	44 (32.6)	313 (44.3)	**0.01**	0
Follow-up (months after surgery)	24.7 SD 11.4	24.1 SD 11.9	24.8 SD 11.3	0.513	0
Any complaints	196 (23.7)	21 (16.3)	175 (25.1)	**0.03**	15
Bulging	108 (12.9)	12 (9.2)	96 (13.6)	0.17	14
Sensation of non-solid scar	88 (10.7)	11 (8.7)	77 (11.1)	0.42	20
Discomfort	144 (17.1)	12 (9.2)	132 (18.7)	**0.01**	15
Discomfort specified (n)	144	12	132	**0.006**	0
Sensitive scar only	6 (4.2)	0 (0)	6 (4.5)		
VRS mild pain/discomfort	68 (47.2)	8 (66.7)	60 (45.5)		
VRS moderate pain	37 (25.7)	3 (25)	34 (25.8)		
VRS severe pain	15 (10.4)	0 (0)	15 (11.4)		
Less sensitivity	14 (9.7)	1 (8.3)	13 (9.8)		
Other discomfort	7 (4.9)	0 (0)	7 (5.3)		
Frequency of discomfort (n)	144	12	132	0.057	23
Rarely	32 (22.2)	6 (50)	26 (19.7)		
Weekly	37 (25.7)	1 (8.3)	36 (27.3)		
Daily	52 (36.1)	2 (16.7)	50 (37.9)		
Not specified	23 (16.0)	3 (25)	20 (15.2)		
Functional limitations due to discomfort (n)	144	12	132	0.052	23
No limitations of general activities	63 (44.4)	8 (66.7)	55 (42.3)		
Some limitations of general activities	30 (21.1)	1 (8.3)	29 (22.3)		
Severe limitations of general activities	26 (18.3)	0 (0)	26 (20)		
Not specified	23 (16.0)	3 (25)	20 (15.2)		

Table 5. Questionnaire results in incisional hernia patients after hernia repair.

VRS: Verbal Rating Scale; Continuous variables are presented a mean and SD, discrete variables are presented as absolute number and (percentage). P for student T-test, fishers exact test or X^2test as appropriate.

Factors associated with postoperative pain and discomfort

Results of multivariable logistic regression are summarized in Table 6. Results of univariable logistic regression are summarized in the Supplement. Current data only provided very limited predictive potential with reference to long-term pain and discomfort (R^2: 0.06). Factors that appeared associated with an increased odds for long-term postoperative pain and discomfort included presence of pre-operative pain and discomfort (OR: 1.74, 95%CI:1.19-2.54), constipation, (OR: 1.61, 95%CI: 1.02-2.55), mesh fixation with use of tackers or staplers (OR: 1.79, 95%CI: 1.28-2.5), and use of a self-adhesive mesh (OR: 2.07, 95%CI: 1.14-3.15).

N = 1298	OR (95%CI)	P	N missing
Age			3
1st quartile	reference		
2nd quartile	1.14 (0.8-1.62)	0.47	
3rd quartile	0.77 (0.53-1.11)	0.16	
4th quartile	0.77 (0.53-1.11)	0.16	
Smoking			96
Never	reference		
Ex-smoker >1 year	0.86 (0.61-1.2)	0.36	
Incidental	0.71 (0.3-1.65)	0.42	
Daily	1.46 (1.01-2.1)	**0.04**	
Constipation	1.61 (1.02-2.55)	**0.04**	
EHS width			50
<4 cm	Reference		
4 – 9 cm	1.22 (0.92-1.16)	0.17	
≥10 cm	1.22 (0.83-1.81)	0.31	
Any pre-operative discomfort	1.74 (1.19-2.54)	**<0.001**	0
Mesh position			19
Sublay (retro-muscular/pre-peritoneal)	reference		
Prefascial onlay	0.51 (0.21-1.25)	0.14	
Intraperitoneal onlay	0.85 (0.63-1.16)	0.30	
No mesh	1.77 (0.54-5.85)	0.34	
Mesh fixation			108
Suture	reference		
Tacker/stapler	1.79 (1.28-2.5)	**<0.001**	
Self-adhesive	2.07 (1.14-3.77)	**0.02**	
No mesh	0.96 (0.29-3.15)	0.94	

Table 6. Multivariable logistic regression, factors associated with long-term postoperative pain and discomfort.

EHS: European Hernia Society. Cases with glue fixation (n=9) and inlay mesh placement (n=5) were excluded from multivariable analysis.

Discussion

Today, it is almost unthinkable to repair an incisional hernia without using a mesh. The mesh is necessary to reinforce the abdominal wall and, subsequently, to prevent incisional hernia recurrence. In spite of the inevitability of mesh reinforcement, resistance against surgical meshes is also present among patients due to potential complications including pain and discomfort. However, considering current literature, there is a lack of evidence concerning the incidences of induced, reduced or maintained pain or discomfort after incisional hernia repair. Additionally, according to several hernia guidelines no recommendation can be made with respect to mesh placement and mesh fixation in reducing postoperative chronic pain [17, 20].

To the best of our knowledge, this is the first study based on prospectively collected data primary investigating these issues in a large sample of patients undergoing various surgical treatments for incisional hernia. Based on the data of the present study, initially asymptomatic incisional hernia patients who undergo surgical repair may develop pain or discomfort in up to 20% of cases. Additionally, pain and discomfort may not always be resolved by incisional hernia repair in initially symptomatic patients. Up to 28% of the latter may continue to experience complaints. Moreover, the initially symptomatic patients experience more severe symptoms after hernia repair compared to the initially asymptomatic patients.

Although the absence of pain or discomfort is considered a relative or even absolute contra-indication for surgical hernia repair, for some patients, the cosmetic appearance of the abdominal wall hernia is a more prominent reason to undergo hernia repair than pain [5]. Nevertheless, in this patient group with no or limited hernia complaints, the risk of inducing pain or discomfort due to surgical repair should be considered when deciding to operate or not. Similarly, in initially symptomatic patients, one should consider that surgical repair will resolve complaints in the majority, but not in all treated patients.

Baseline patient characteristics in this cohort showed some interesting differences between pre-operative symptomatic and asymptomatic patients. Patient with a symptomatic incisional hernia were more likely to be female and were more likely to have a slightly higher BMI. Factors related to an

increased intra-abdominal pressure, such as chronic cough and constipation, were also more frequently reported in symptomatic patients (Table 1). These differences in sex and comorbidities with regard to pre-operative pain were previously reported and warrants further investigation [21].

Another interesting finding is the relation between pre-operative pain complaints and hernia location. Subcostal or suprapubic located incisional hernias more often caused complaints compared to the other hernia sites. An explanation could be found in the distribution of sensory nerve fibers in relation to the length of the incisions. Another hypotheses could be that the edges of the costal and pubic bones might provoke more pain complaints, especially when exercising, due to the more statistical nature of the bone in contrast to the high mobility of the abdominal wall.

Considering severity of reported symptoms in the present cohort, the absence of pain or discomfort may be considered a relative but probably not an absolute contra-indication for surgical hernia repair. For example, if during conservative management a continuous increase of the diameter of the incisional hernia is noted, repair may be considered. Although, pain and discomfort, may be induced in approximately 10-20% of asymptomatic patients, reported complaints were usually minor, i.e. mild pain in 66.7% of patients (n=12) after a mean follow-up of 24.1 months postoperatively. Aesthetic complaints, leading to functional limitations may very well outweigh this risk in selected patients.

Another reason to repair a ventral hernia is the risk for incarceration. Previous studies reported prevalence rates of incarceration between approximately 3 and 10% [22-24]. Mostly defects of approximately 3 to 4 cm in width appeared prone for incarceration [25]. In this respect, for asymptomatic patients with multiple potential risk factors for incarceration, elective hernia repair could be beneficial as a preventive measure. In other non-complex ventral hernia patients, watchful waiting is mostly considered a safe strategy [26-28]. However, one previous study reported high crossover rates with significantly greater incidences of intraoperative perforations, fistulas, emergency surgery, and mortality due to watchful waiting [29]. Nevertheless, according to the Guidelines for laparoscopic treatment of primary ventral and incisional abdominal wall hernias, watchful waiting is recommended in patients with modifiable risk factors [20].

Hitherto, no recommendations in surgical technique or surgical accessory as suture, tacker, glue or mesh type could be made regarding the incidence of chronic pain [20]. Considering our current results, predicting the occurrence of chronic pain based on patient and surgical characteristics appears difficult indeed. Although detailed information was available concerning patient and surgical characteristics, it was not possible to construct a model with sufficient predictive power, to substantiate any meaningful recommendations. Considering the observational design of current study, these associations must be interpreted with great caution.

Based on the sample at hand, mesh repair was not significantly associated with long-term pain or discomfort, as compared to suture repair. Additionally, the position of the surgical mesh appeared not associated with long-term pain either. However, patients with an incisional hernia, who received an intraperitoneal onlay mesh (IPOM), appeared to present slightly more often with a symptomatic incisional hernia (Table 2).

In contrast, the method of mesh fixation appeared associated with long-term pain and discomfort. According to the data presented in this study, both the use of tackers and self-adhesive meshes were associated with increased odds for long-term postoperative pain and discomfort. These observations have been previously hypothesized and reported.

From performing abdominal surgery under local anesthesia in the late 19th and begin 20th century, the parietal peritoneum is known to be intensively sensitive to pain [30]. New studies confirmed these early observations. Additionally, the parietal peritoneum is sensitive to pressure, touch, friction, cutting and temperature through innervation by the phrenic and sensitive spinal (lower thoracic) viscero-somatic nerves [31]. Attaching a mesh to the peritoneum with tackers, might stimulate these nerve fibers leading to pain sensation.

The mesh must be fixated on the abdominal wall to prevent migration and to maintain good contact between abdominal wall and mesh. Bansal *et al.*[32] compared suture mesh fixation *versus* tacker mesh fixation for laparoscopic repair of ventral hernias in a prospective randomized study. This study found, similar to the current observational report, that the use of suture fixation was more beneficial with respect to postoperative pain [32]. The authors

hypothesized that tackers may cause increased incidence of pain due to the screwing mechanism of the sharp tips penetrating the tissue and thereby causing compression and twisting of nerve fibers [32]. Additionally, tackers are approximately seven times more costly compared to conventional suture fixation [33].

Until now, no pathophysiologic mechanism of self-adhesive meshes inducing postoperative chronic pain is known. Possibly, self-adhesive meshes may cause a peritoneal tissue reaction [34]. Self-adhesive meshes are relatively new and not studied thoroughly for ventral hernia repair. One retrospective single-arm cohort study of Kroese *et al.*[35] found that 9 out of 39 patients (23%) reported pain complaints (mean VAS=1.7) after open complex abdominal wall hernia repair with the self-adhesive ProGrip™ mesh after a median follow-up of 25 months. However, no pain was reported by Bueno-Lledó *et al.*[36] six months after using self-adhesive ProGrip™ mesh in Rives-Stoppa repair.

Considering current outcomes, incisional hernia research should emphasize more on functional outcomes, in addition to treatment success in terms of recurrence rates. Pain and discomfort after prophylactic mesh reinforcement warrants further evaluation.

Limitations

This cohort study has several limitations. Pain and discomfort, although collected by standardized scores and questionnaires, remain subjective measurements and probably differ over time. Additionally, data on functional limitations as a result of pain and discomfort were only available in a subset of patients. Although data was collected in a prospective manner, this study remains observational, therefore causality of found associations cannot be confirmed. Therefore, current data should be interpreted with caution. Nevertheless, the sample at hand may represent the general patient population undergoing surgical incisional hernia repair, as seen in every day clinical practice. Although this introduces some heterogeneity, this sample is not limited to one technique or a certain subset of complex patients. However, it is important to realize that all surgical procedures were performed by dedicated abdominal wall surgeons. This introduces some selection bias as the sample may consist partly of secondarily referred patients. Therefore, these results mostly translate to the practice of a dedicated hernia surgeon.

Conclusion

Incisional hernia complaints may be resolved in the majority of cases after surgical repair. However, in asymptomatic incisional hernia patients, pain or discomfort may be induced in a considerable number of patients due to surgical repair and one should be aware if this postoperative complication. Symptomatic hernia patients should be informed that surgical repair may resolve pain or discomfort in the majority, but not all patients.

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Supplemental materials

N = 1297	OR (95%CI)	P	N missing
Age			3
1st quartile	reference		
2nd quartile	1.16 (0.82-1.63)	0.40	
3rd quartile	0.75 (0.52-1.06)	0.10	
4th quartile	0.74 (0.52-1.05)	0.09	
Female sex	1.06 (0.82-1.35)	0.65	
BMI (kg/m^2), per one increase	0.99 (0.97-1.01)	0.41	24
Smoking	0 (0-0)	**<0.001**	96
Never	reference		
Ex-smoker >1 year	0.85 (0.62-1.17)	0.31	
Incidental	0.68 (0.29-1.57)	0.36	
Daily	1.67 (1.18-2.36)	**<0.001**	
Constipation	1.63 (1.04-2.54)	**<0.001**	18
Corticosteroids	0.5 (0.23-1.07)	0.08	16
Diabetes mellitus	0.79 (0.56-1.11)	0.17	16
Chemotherapy	0.69 (0.45-1.07)	0.10	16
Previous mesh surgery	1.06 (0.8-1.36)	0.75	16
ASA III-IV	0.88 (0.67-1.17)	0.39	9
Hernia location			17
Subxiphoid	reference		
Epigastric	0.63 (0.31-1.25)	0.18	
(peri)Umbilical	0.63 (0.33-1.2)	0.16	
Infra-umbilical	0.67 (0.34-1.32)	0.25	
Suprapubic	0.78 (0.37-1.64)	0.51	
Only lateral	0.6 (0.3-1.18)	0.13	
EHS width			50
<4 cm	reference		
4 – 9 cm	1.24 (0.94-1.63)	0.12	
≥10 cm	1.23 (0.85-1.79)	0.27	
Incarceration (non-reducible)	1.24 (0.56-2.75)	0.59	10
Synchronous repair of multiple defects	1.21 (0.86-1.7)	0.27	18
Any pre-operative discomfort	1.67 (1.16-2.41)	**0.01**	0
Emergency surgery	1.66 (0.94-2.93)	0.08	8

N = 1297	OR (95%CI)	P	N missing
Mesh position			19
Sublay (retro-muscular/pre-peritoneal)	reference		
Prefascial onlay	0.77 (0.33-1.8)	0.54	
Intraperitoneal onlay	0.95 (0.73-1.24)	0.72	
No mesh	1.39 (0.89-2.15)	0.14	
Mesh fixation			108
Suture	reference		
Tacker/stapler	1.57 (1.16-2.14)	**0.00**	
Self-adhesive	1.88 (1.07-3.29)	**0.03**	
No mesh	1.65 (1.07-2.55)	**0.02**	
Laparoscopic surgery	1.21 (0.84-1.75)	0.30	15

Table 1. Univariable logistic regression, factors associated with long-term postoperative pain and discomfort.

BMI: body mass index; ASA American Society of Anesthesiologists; EHS: European Hernia Society.

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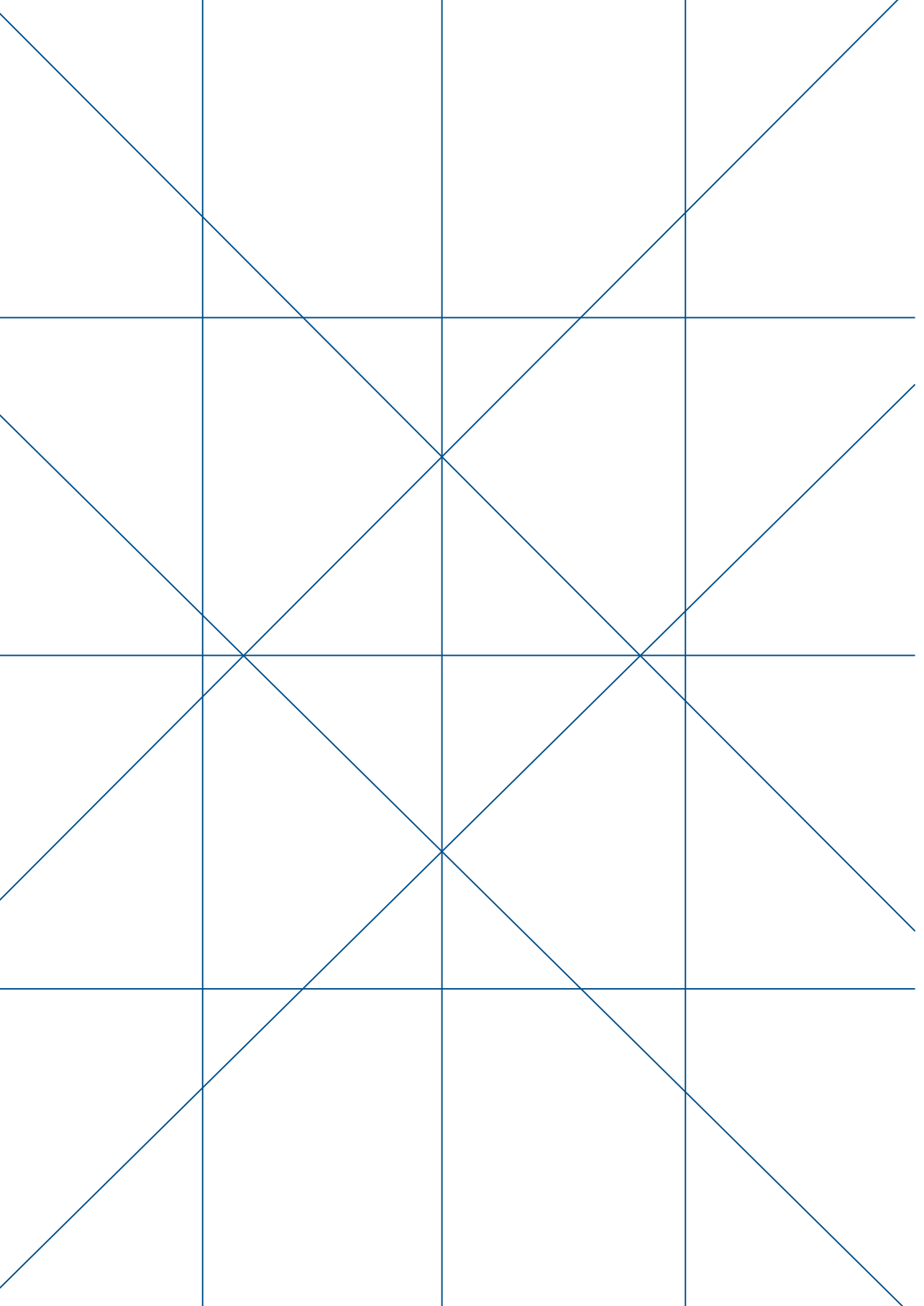

Chapter 10

General discussion and future perspectives

An abdominal wall hernia is a benign but frequently appearing condition. Researchers from around the world are trying to improve the knowledge regarding this subject on a large scale. In this thesis, the prevention and treatment of abdominal wall hernia are investigated in an attempt to increase the surgeon's knowledge and understanding of the closure of the *linea alba*.

Small bites versus large bites technique for linea alba closure

Clinical research has shown the superiority of the use of a suture length to wound length ratio of at least four to one (*i.e.* small bites) for the closure of the linea alba [1, 2]. However, the incidence of incisional hernia remains high [3]. An epidemiological explanation is represented by the change in the patient population undergoing open repair, due to the introduction of laparoscopic repair for example, resulting in a patient group more prone to the development of incisional hernia. The incidence of incisional hernia and recurrence remains high despite improved surgical techniques over the past decades. Knowledge of the biomechanical mechanisms explaining the superiority of the small bites technique compared with the large bites technique is scarce. An attempt at filling this gap in knowledge was the rationale behind the first part of this thesis. An important part of understanding and improving closure configurations for the *linea alba* is studying the biomechanical behavior of the intact abdominal wall. Closure configurations which closely simulate the 'behavior' of the intact abdominal wall should be suggested and tested. In addition to this, manufacturers should improve current mesh types in order to make them mimic the natural (mechanical) behavior of the abdominal wall as much as possible. However, this has proven to be challenging as earlier research has shown that collagen formation alters the original mesh characteristics [4].

Understanding the biomechanical behavior of the abdominal wall was attempted by estimating strain patterns on the fascia of the abdominal wall for several closure configurations. This was performed by using a speckle pattern and a digital image correlation-based model in a passive model with *post mortem* human specimens. Digital image correlation is a visual method for tracking alterations on the surfaces of materials, for measuring strains and displacement [5]. Digital image correlation is popular and extensively used

mainly in mechanics for regular or polymeric metals [6]. Earlier research has used this method on the fascia of human and porcine abdominal wall, however, these experiments and the present experiment are only the first steps in using this method for the human fascia [7, 8]. In the present work, no differences were found between small and large bites; however, a stiffer behavior of the abdominal wall was observed when a mesh was placed in onlay position. This experiment has several shortcomings. Inflation of the abdominal cavity could have been done whilst simultaneously inflating the lungs, in order to keep the diaphragm at its place to imitate physiology. Additionally, contraction of abdominal wall muscles could have been simulated, creating a different experimental model. Options other than post mortem human specimens are, for example, ex vivo porcine or human abdominal walls and the 'AbdoMan'. The 'AbdoMan' is a computerized device simulating the human abdominal wall, combining intra-abdominal pressure with muscle contractions [9]. Notwithstanding, in retrospect, this device would not have been fully suitable for understanding strain patterns on the abdominal wall fascia, since boundary conditions, such as the ribs, the pelvis and the insertions of the muscles, would be missing. These factors could have influenced the results, although we do not know to what extent. We should be aware of the fact that this present research is only a tiny part of a complicated puzzle. Another known contributing factor for the occurrence of burst abdomen and the formation of an incisional hernia, besides of strain distribution on the abdominal wall, is suture tension [10]. Suture tension may be too low or too high, and consequently not be optimal, resulting in acute wound problems (burst abdomen) or an impaired wound healing process (incisional hernia). It is well-known that surgeons, thinking that they apply the exact same tension on each knot while suturing, in reality still apply various levels of tension [11]. In addition, variability between different surgeons is high, which makes measuring suture tension during suturing a relevant factor in prevention. However, to the best of our knowledge, no (clinical) suture strain gauge is available on the market at this moment. In this thesis, a custom-made suture tension sensor was made and used in an experimental setting. In this present experimental set-up, the newly developed suture material, Duramesh™, is the only material which has been tested comparing small bites with large bites. In the ideal situation, the optimal window of applied tension for different tissue types and suture

materials would be known beforehand. The best scenario would be to measure the tension during the suturing process, instead of after the suturing process, in living animals or humans, while intra-abdominal pressure is varied at different timeframes.

The experimental treatment of complex abdominal wall hernias

Post mortem human specimens are a good model for abdominal wall hernia repair experiments. Despite a few known limitations, such as the absence of muscle contractions, varying intra-abdominal pressure - and maybe most importantly – the absence of wound healing, the use of post mortem human specimens is incredibly useful in the anatomical-biomechanical aspects of hernia research. In an anatomical study in this thesis, a comparison was made between the anterior and posterior component separation operation techniques and the subsequently obtained medialization of the anterior and posterior rectus fascia. Both anterior and posterior component separation measurements were performed in each post mortem human specimen, one technique per side of the abdominal wall, causing each specimen to act as its own control sample. Obviously, this experiment could never have been performed in living humans. Nonetheless, this study gives hernia surgeons important insights in these known and newly developed repair techniques and what they may achieve by performing it. Recent evidence demonstrated that a combination of both anterior and posterior component separation techniques for the repair of a giant hernia in one patient could be helpful for tension-free repair [12]. Other than post mortem human specimens, animal models are available and useful in abdominal wall hernia research. For example, newly developed meshes used in abdominal wall hernia repair cannot be implanted in humans without being tested in an animal model first. Testing meshes in animals is of paramount importance, since histological, biomechanical and immunological parameters can never be analyzed ethically in living humans. A limitation is the fact that research with animals cannot be directly translated to humans. Additionally, we are well aware of the fact that there is a lack of comparability between all available abdominal wall hernia animal models. Currently, research is being conducted to improve the comparability of animal research in order to become more valuable.

The prevention and treatment of abdominal wall hernias in clinical settings

Fundamental, experimental research is, as the word itself says, the fundament of all research and of outstanding importance for clinical practice. This thesis was largely based on fundamental research and understanding the basics of abdominal wall repair, in order to provide input for the clinical perspective. The last part of this thesis focused on several clinical research questions for improving hernia care in living patients.

Our study was based on the extensive French abdominal wall hernia repair registry, collected by almost 50 members of the 'Club Hernie' (the French Hernia Club). Abdominal wall hernias with a defect width of three to four centimeters were mainly associated with incarceration. Surgeons and teachers have always taught fellows and residents that smaller hernias are more prone for incarceration; however, evidence for this statement, other than common sense, was missing. Answering this clinically relevant research question regarding incarceration risk and hernia width with an observational study has its drawbacks. A general drawback of this registry-based study is that patients were only included in case surgical repair was performed by a member of the Hernia-Club; non-repaired hernias were not included in the database and consequently, not included in in the analysis. An additional drawback is that abdominal wall hernias repaired in an emergency setting (with incarceration or strangulation) are more likely to be operated by a regular surgeon and not a member of the Hernia-Club, and are therefore not included in the database, possibly resulting in a biased overview.

An interesting and challenging group of patients are patients with giant primary or incisional hernias. These types of abdominal wall hernias with loss of domain are defined as a radiologically measured ratio of the volume of the incisional hernia to the volume of the abdominal cavity of more than 20 percent [13]. Repair of giant hernias with loss of domain is associated with postoperative complications such as abdominal compartment syndrome and respiratory problems. Botulinum toxin A and/or preoperative progressive pneumoperitoneum are available to aid in the repair of giant hernias, as an addition to the existing component separation techniques. In our series with 23

patients, botulinum toxin A was safe to use, however preoperative progressive pneumoperitoneum resulted in complications in 21% of all patients. In a recent retrospective cohort of 100 patients with a giant hernia with loss of domain undergoing hernia repair, the combination of those two techniques was advantageous and appeared to be safe [14]. Prospective studies are still highly needed in order to create a preoperative algorithm to find out which patients will benefit from these preoperative aids.

Since the introduction of a prosthetic mesh for the repair of chest and abdominal wall defects in 1959 by Usher, the use of meshes has become standard care for abdominal wall hernia repair [15, 16]. Before the introduction of mesh-based repair, the high recurrence rate was the most common and feared complication after abdominal wall hernia repair. The recurrence rate has been reduced dramatically by the introduction of mesh augmented repair. Mesh-augmented abdominal wall hernia repair is mainly applied in patients with a symptomatic hernia. However, there are reasons to repair an abdominal wall hernia in patients without symptoms. The implantation of meshes in abdominal wall hernia repair is considered standard care, although this is not without its drawbacks, since meshes are associated with chronic pain, infection and fistula formation for example [17, 18]. It was shown in this thesis, that 28 per cent of all pre-operatively symptomatic patients and 20 per cent of all pre-operatively asymptomatic patients with incisional hernia will develop or have persisting pain or discomfort complaints. The risks of developing these postoperative complications should always be discussed with all patients preoperatively.

Future perspectives

Despite extensive work by researchers around the world on both prevention and treatment of abdominal wall hernias, many questions are left unanswered.

An option for measuring the displacement and strains of the mesh could be the use of a bionic mesh; a ‘smart mesh’, with interwoven electrodes or strain gauge-like sensors. Such a mesh would allow to remotely monitor the position of the mesh and, possibly, get an in-depth understanding of the etiology of an incisional hernia. Another possibility is to implant a small sensor next to the sutured fascia in order to directly receive information regarding strains

and wound healing. For the foreseeable future, these options would only be possible in living animal models. In the near future, the custom-made suture tension sensor as developed in this thesis can be used in more and different experimental settings in order to test existing or new suture materials and suturing configurations or techniques. The suture tension sensor could be waterproofed in order to be used for longer experiments in animal models. The next step would be to create a surgical instrument or surgical thread which changes color while using it. The instruments or the materials could turn green, red or any preferred color to indicate the tension applied to the suture.

The 'AbdoMan' is a promising tool for performing research on laparotomy closure, especially because it reduces the number of test animals used for scientific research, while being able to perform largely the same experiments. Hernia researchers could improve this existing abdominal wall model. The abdominal wall that is currently used on the 'AbdoMan' is made of a single layer of synthetic material, which was created to mimic the average direction of the muscle fibers of the human abdominal wall.

A next step could be to create an artificial abdominal wall with several different fiber directions. Attempts to replace test animals by synthetic material mimicking the human abdominal wall have been performed by our group, but until now the created tissue was not broadly used in research [19]. Ideally, the 'AbdoMan' would be extended with a thoracic cavity, for simultaneous inflation of both the abdominal and the thoracic cavities. As such, not only horizontal, but also vertical loads on the midline can be considered with the inflation of the lungs. Artificial intelligence could brighten the future of abdominal wall hernia research as well, allowing us to predict strains and to model ischemia and wound healing, substituting in-vivo tissue for algorithms and data.

From a clinical perspective, it is apparent that surgeons have difficulty implementing new techniques in their daily practice. Since the introduction of the suture length to wound length ratio of at least four by Jenkins in 1976 and much clinical evidence later proving the benefit of the small bites technique in decreasing the occurrence of incisional hernia, surgeons are still using historical techniques. Surgeons could be reluctant for using the small

bites technique for fear of fascia dehiscence (also ‘Platzbauch’), one of the most disastrous outcomes of open abdominal surgery. Implementation seems difficult and time consuming. The fact that non-abdominal wall surgeons perform laparotomies and abdominal wall fascia closures makes it even more challenging to implement this knowledge. An option for implementing the small bites techniques could be by inviting all surgeons operating in the abdominal cavity (i.e. urologists and gynecologists) to meetings or congresses explaining the importance of this topic. Social platforms are helpful in spreading the information as well. Another option is that younger fellows or doctors in training with abdominal wall interest make their teachers aware of these new insights in closure. Whether this kind of surgery should be performed in centralized and specialized centers is subject of debate and for a large part dependent on national initiatives and hence on political decision making.

Finally, as in all research, communication and cooperation between researchers is of paramount importance. Unfortunately, until now, scientific societies have not been able to stimulate their members enough to coordinate all research in the field. Additionally, as a result of how academic centers are financed, scientific societies are obliged to develop their own individual research programs. It would be of great benefit if research programs are defined by the scientific societies, at which private and governmental grants can be directed.

In closing, it is becoming more and more apparent that the only way forward is to close the chasm between science and clinics. These two, which are often still seen as two different paths, should be seen as two sides of the coin and researchers and clinicians should join their efforts in order to further improve the quality of healthcare in general and more specifically of surgery.

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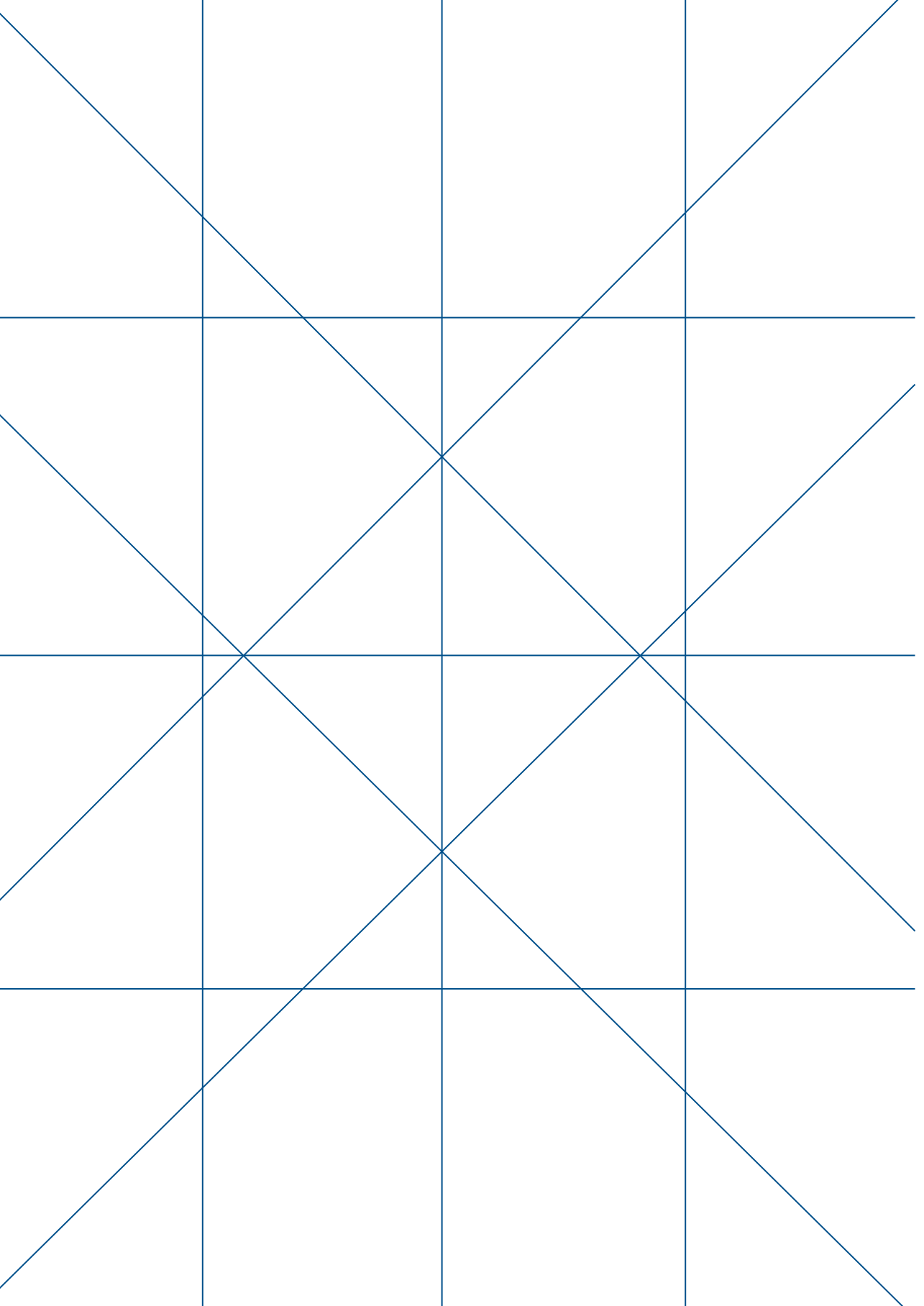


Chapter 11

Summary

This thesis focused on improving closure techniques for the linea alba and subsequently preventing incisional hernia formation. Additionally, treatments for giant and contaminated abdominal wall hernias were studied in several experiments. Finally, clinical questions regarding prevention, risk for incarceration and the treatment of (mainly) incisional hernias were answered.

First, a general introduction on risk factors, prevention and treatment of abdominal wall hernia was given in **Chapter 1.**

Underlying biomechanical mechanisms for the closure of the abdominal wall were investigated in ***Part 1*** of this thesis.

In **Chapter 2**, a digital image correlation-based method was used to compare strain fields on the abdominal wall of post mortem human bodies between the intact linea alba and five linea alba closure configurations, including a polypropylene mesh placed in onlay position. All comparisons were made just after surgical closure in a passive *post mortem* model. No visible differences were found between small bites (five millimeters from the wound edge and five millimeters between two stitches) and large bites (ten millimeters from the wound edge and ten millimeters between two stitches) with this digital image correlation-based method. In addition, the midline showed more stiff behavior when a mesh was placed after fascia closure with large bites. This finding is in contrast with earlier clinical findings, in which small bites resulted in less incisional hernias in comparison with large bites. Reasons for not reaching the same conclusions could be due to the passive (i.e. no muscle contractions, no breathing simulation) and post mortem experimental design.

In **Chapter 3**, the measuring of suture tension in small and large interrupted sutures for the closure of six ex vivo porcine abdominal wall was described. A custom-made suture tension sensor was developed for suture tension measurement in these experiments. An artificial and inflatable abdominal wall, named the 'AbdoMan' was used to fixate a porcine abdominal wall. Additional to the comparison between small and large bites with the use of conventional suture material (PDS II 2-0), a newly developed suture material was tested. Duramesh™, created from strips of uncoated macroporous polypropylene mesh, was used to investigate suture tension. Small bites were more efficient at dividing the suture tension across the incision compared to large bites with the use of both suture materials. However, Duramesh™ was not significantly different when compared with a conventional suture material.

In ***Part 2*** the treatment of giant and contaminated abdominal wall hernias was investigated in experimental set-ups.

In **Chapter 4**, a total of 10 post mortem human specimens were first treated with the Rives-Stoppa technique and subsequently with the anterior and posterior component separation techniques. The aim of this study was to compare additional medialization after initial opening of the linea alba in one post mortem human specimen, performing both component separation techniques. This study was performed in an experimental setting, since these calculations and comparisons cannot be made in living humans. Medialization was measured at three levels with one- and two-kilogram weights. Significantly more medialization was achieved on the posterior rectus fascia after performing the posterior component separation technique. In these experiments, medialization was not significantly different on the anterior rectus fascia between both component separation techniques. In conclusion, both techniques may be used for the repair of giant (^{3} ten centimeters) abdominal wall hernia.

In **Chapter 5** a study in which zinc-impregnated polypropylene and control polypropylene meshes without zinc impregnation were implanted intraperitoneally in 38 rats with induced peritonitis is described. The aim of this study was to find out whether zinc impregnation will result in a lower number of colony forming units on a sample (mesh and abdominal wall). Rats were sacrificed after 30 and 90 days. A lower number of colony forming units per sample was seen in the zinc group in comparison with the control group on one out of two types of agar plates after 90 days. No differences between the groups were seen after 30 days. An important secondary finding was the higher percentage of adhesions on the mesh surface in the rats with a zinc-impregnated polypropylene mesh in comparison with the control meshes after 90 days of follow-up. An important note with regard to the occurrence of adhesions is that this was not the primary endpoint and it was measured in a subjective way. One may conclude that these findings regarding the zinc-impregnated mesh suggest antibacterial properties when placed in a contaminated environment. This should encourage researchers to perform more research.

In ***Part 3,*** prevention and treatment were investigated including simple and complex abdominal wall hernia.

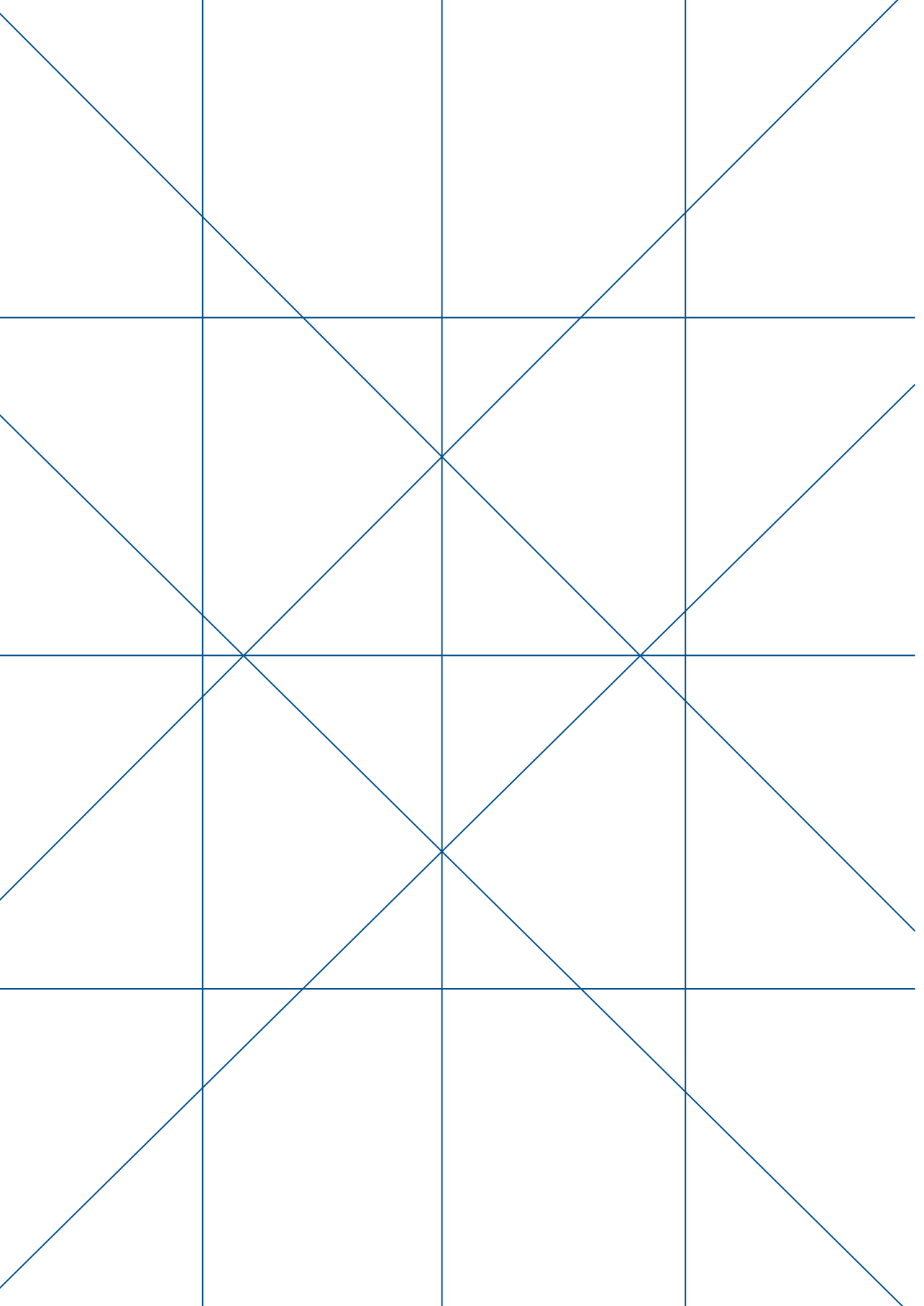
In **Chapter 6** a literature review was performed on the prevention of incisional hernia. Risk factors may be split into patient and surgery related determinants. Enhancing surgical techniques and materials has the potential to prevent incisional hernia formation and subsequently reduce healthcare costs. Mass closure with a continuous technique and a suture length to wound length ratio of four or more (small bites) using slowly or non-absorbable sutures are recommended in this chapter. Surgical site infections are a known risk factor for the development of incisional hernia and should as such be prevented. Additionally, in known high-risk patients, a prophylactic mesh should be considered for the closure of the midline after laparotomy. Lastly, modifiable risk factors on patient level, such as smoking an HbA1c levels higher than 7% (53 millimole per mole), should be optimized pre-operatively.

Chapter 7 describes a prospective, registry-based study for the assessment of the relation between primary abdominal wall hernia (n = 2352) and incisional hernia (n = 2120) with incarceration and defect size, as well as defect location. The prevalence of a non-reducible incarceration was 3.5 percent in primary abdominal wall hernia and 3.7 percent in the incisional hernia group. In this study was found that for both types of hernias, defects of three to four centimeters were associated with incarceration and hernias smaller than two centimeters incarcerate rarely. Notable is that in patients with primary abdominal wall hernia, ten percent of all patients with a hernia defect size between three to four centimeters presented with incarceration. Additionally, peri- and infra-umbilical hernias were associated with incarceration only when these are primary abdominal wall hernias. Age, body mass index (BMI), and factors related to increased intra-abdominal pressure were examples of variables which are also associated with hernia incarceration. Interestingly, female sex was associated with incarceration only in patients with incisional hernia. An evidence-based reason for this finding remains unfound.

Chapter 8 describes a case series of 23 patients with giant primary or incisional hernias with or without loss of domain treated with botulinum toxin A, preoperative progressive pneumoperitoneum (Goni-Moreno technique) and component separation techniques. The combination of botulinum toxin A injections and preoperative progressive pneumoperitoneum may be helpful for tension-free fascial closure in patients with giant abdominal wall hernia

in addition to component separation techniques. However, it is challenging to know beforehand, preoperatively, which patient will need these preoperative aids. In this present cohort, a standardized preoperative algorithm was developed for patients with a giant hernia to prevent the surgeon from unforeseen difficulties during the operation. After a median follow-up of 19.5 months, primary anterior fascia closure was possible in 82% of all patients with the use of this algorithm. Three patients had a hernia recurrence and 16 patients had surgical site occurrences, mainly being surgical site infections. It should be kept in mind that almost all patients in this cohort suffered from obesity and other comorbidities.

In **Chapter 9** functional outcomes in symptomatic and asymptomatic patients with incisional repair were investigated based on a prospective, registry-based cohort. Despite the fact that incisional hernia repair with mesh mostly results in resolving symptoms, repair may likewise induce or cause existing pain to persist. Pre-operatively symptomatic patients (n = 1091) reported pain or discomfort after hernia repair in 28% of all cases, after a mean follow-up of 11.3 months. Pre-operatively asymptomatic patients (n = 221) reported pain or discomfort after hernia repair in 20% of all cases after a mean follow-up of 10.5 months. In conclusion, pain and discomfort will be resolved in most cases of incisional hernia repair. This risk of inducing pain or discomfort in preoperatively asymptomatic patients should be discussed thoroughly with the patient when deciding for repair. Additionally, symptomatic patients should be informed on the risk of persisting symptoms after surgical repair.



Chapter 12

Samenvatting

Dit proefschrift richt zich op het verbeteren van sluitingstechnieken voor de linea alba en het voorkomen van buikwandbreuken, voornamelijk littekenbreuken. Daarnaast wordt in verschillende experimenten de behandeling van extreem grote en gecontamineerde buikwandbreuken bestudeerd. Tenslotte is gepoogd enkele klinische vraagstukken rondom preventie, incarceratierisico en behandeling van (voornamelijk) littekenbreuken te beantwoorden.

In **Hoofdstuk 1** wordt over de ontwikkeling, preventie en behandeling van buikwandbreuken een algemene inleiding gegeven.

Biomechanische mechanismen die ten grondslag liggen aan verschillende sluitingstechnieken voor de *linea alba* werden in ***Deel 1*** van dit proefschrift onderzocht.

In **Hoofdstuk 2** wordt een op *digital imaging correlation* gebaseerde methode gebruikt om de spanningsverdeling op de buikwand van *post mortem* menselijke lichamen te vergelijken met een intacte *linea alba* en vijf verschillende sluitingstechnieken met ook een onlay geplaatste polypropyleen mat. Alle vergelijkingen werden direct na chirurgie in een passief en p*ost mortem* model gemaakt. Met de op *digital imaging correlation* gebaseerde methode werd geen zichtbaar verschil gevonden tussen *small bites* (per 5 millimeter een hechting met 5 millimeter afstand van de wondrand) en *large bites* (per 10 millimeter een hechting met 10 millimeter afstand van de wondrand). Wel was gebleken dat de buikwand bij het *onlay* plaatsen van een polypropyleen mat na het sluiten met *large bites* stijver is. Deze bevindingen staan in contrast met bevindingen uit klinische studies waarbij *small bites* in vergelijking met *large bites* na een jaar *follow-up* in minder littekenbreuken resulteerden. Redenen voor deze discrepantie kunnen zijn dat de passieve (ontbreken van spiercontracties en simulatie van de ademhaling bijvoorbeeld) en *post mortem* inrichting van dit experiment.

In **Hoofdstuk 3** wordt een onderzoek beschreven waarin de hechtrdaadspanning werd gemeten met enkelvoudige *small bites* en *large bites* voor het sluiten van zes *ex vivo* varkensbuikwanden. Een op maat gemaakte hechtdraadspanningssensor werd ontwikkeld voor het meten van de hechtdraadspanning in deze experimenten. De varkensbuikwanden werden daarbij vastgeklemd op een artificiële en opblaasbare buikwand, genaamd

de ‘AbdoMan’. Behalve de vergelijking tussen *small* en *large bites* met het gebruik van conventioneel hechtmateriaal (PDS II 2-0) werd ook een nieuw ontwikkeld type hechtmateriaal getest. Het nieuwe hechtmateriaal Duramesh™ is gemaakt van niet-gecoate stroken van een macroporeuze polypropyleen mat en zou de spanning beter verdelen in vergelijking met conventioneel hechtmateriaal zoals PDS II 2-0. In dit experiment bleken *small bites* meer efficiënt te zijn in het verdelen van de hechtingdraadspanning over de incisie in vergelijking met large bites in beide materialen. Duramesh™ was echter niet significant beter in het verdelen van de spanning vergeleken met conventioneel hechtmateriaal.

In ***Deel 2*** werd de behandeling van extreem grote en gecontamineerde buikwandbreuken experimenteel onderzocht.

In **Hoofdstuk 4** wordt de operatie van in totaal 10 *post mortem* menselijke lichamen beschreven door allereerst de Rives-Stoppa techniek uit te voeren en vervolgens de anterieure en posterieure component separatie techniek. Het doel van dit onderzoek was om additionele medialisatie na initiële incisie van de *linea alba* te meten en te vergelijken na beide component separatie technieken in *post mortem* menselijke lichamen. Deze studie werd uitgevoerd in een experimentele opstelling omdat deze berekeningen en vergelijkingen niet gemaakt konden worden in de klinische *setting*. Medialisatie van de rectusspier werd op drie verschillende anatomische niveaus met gewichten van één en twee kilogram gemeten. Er was significant meer medialisatie van de posterieure rectus fascie na de posterieure separatie techniek verkregen. In deze experimenten was de medialisatie van de anterieure rectus fascie niet significant verschillend tussen de anterieure en posterieure component separatie technieken. Concluderend zijn beide technieken geschikt voor het herstel van extreem grote (≥ 10 centimeter) buikwandbreuken.

In **Hoofdstuk 5** wordt een experiment beschreven waarbij polypropyleen matten met en zonder zink impregnatie bij 38 ratten met geïnduceerde peritonitis intraperitoneaal werden geplaatst. Het doel van dit onderzoek was onder andere om uit te zoeken of er, in met zink geïmpregneerde polypropyleen matten, minder kolonievormende eenheden op een monster (bestaande uit mat en buikwand) te vinden zouden zijn. De ratten werden na 30 en 90 dagen geofferd. Een lager aantal kolonievormende eenheden per monster

werd in de groep ratten met zink geïmpregneerde matten in vergelijking met de controlegroep gevonden na 90 dagen en op een van de twee typen agar platen. Er werd geen verschil gevonden na 30 dagen tussen beide groepen. Een belangrijke andere bevinding in deze studie was echter dat er een hoger percentage adhesies bij de ratten met een zink geïmpregneerde polypropyleen mat in vergelijking met de controlegroep gevonden werd. Het is belangrijk om te beseffen dat het bepalen van adhesies niet een primair eindpunt was. Daarnaast werden de adhesies in dit experiment op een subjectieve wijze gemeten. Dit resultaat zou daarom met voorzichtigheid geïnterpreteerd moeten worden. Concluderend zouden deze bevindingen kunnen wijzen op mogelijke antibacteriële eigenschappen van de polypropyleen matten met zink impregnatie in geval van (mogelijke) contaminatie. Dit resultaat kan onderzoekers aanzetten tot onderzoek naar deze specifieke matten.

In ***Deel 3*** werd de preventie en de behandeling van eenvoudige en complexe buikwandbreuken onderzocht.

In **Hoofdstuk 6** is een overzicht van de literatuur over de verschillende manieren van preventie van littekenbreuken gegeven. Risicofactoren kunnen worden onderverdeeld in patiënt- en operatie gerelateerde factoren. Verbetering van chirurgische technieken en hechtmaterialen kan littekenbreuken voorkomen en zo de kosten voor de gezondheidszorg verminderen. In dit hoofdstuk wordt aanbevolen om de fascie met behulp van een doorlopende hechttechniek, zonder aparte sluiting van het peritoneum, in één laag te sluiten, waarbij de langzaam of niet-resorbeerbare hechtdraad minimaal viermaal zo lang is als de lengte van de incisie (*small bites*). Postoperatieve wondinfectie is een bekende risicofactor voor het ontstaan van een littekenbreuk en moet daarom waar mogelijk voorkomen worden. Daarbij zou bij patiënten met een hoog risico op het ontwikkelen van een littekenbreuk na een laparotomie in de middenlijn een profylactische mat overwogen moeten worden. Ten slotte moeten beïnvloedbare risicofactoren op patiëntniveau, zoals roken of een HbA1c-spiegel hoger dan 7% (53 millimol per mol), preoperatief worden geoptimaliseerd.

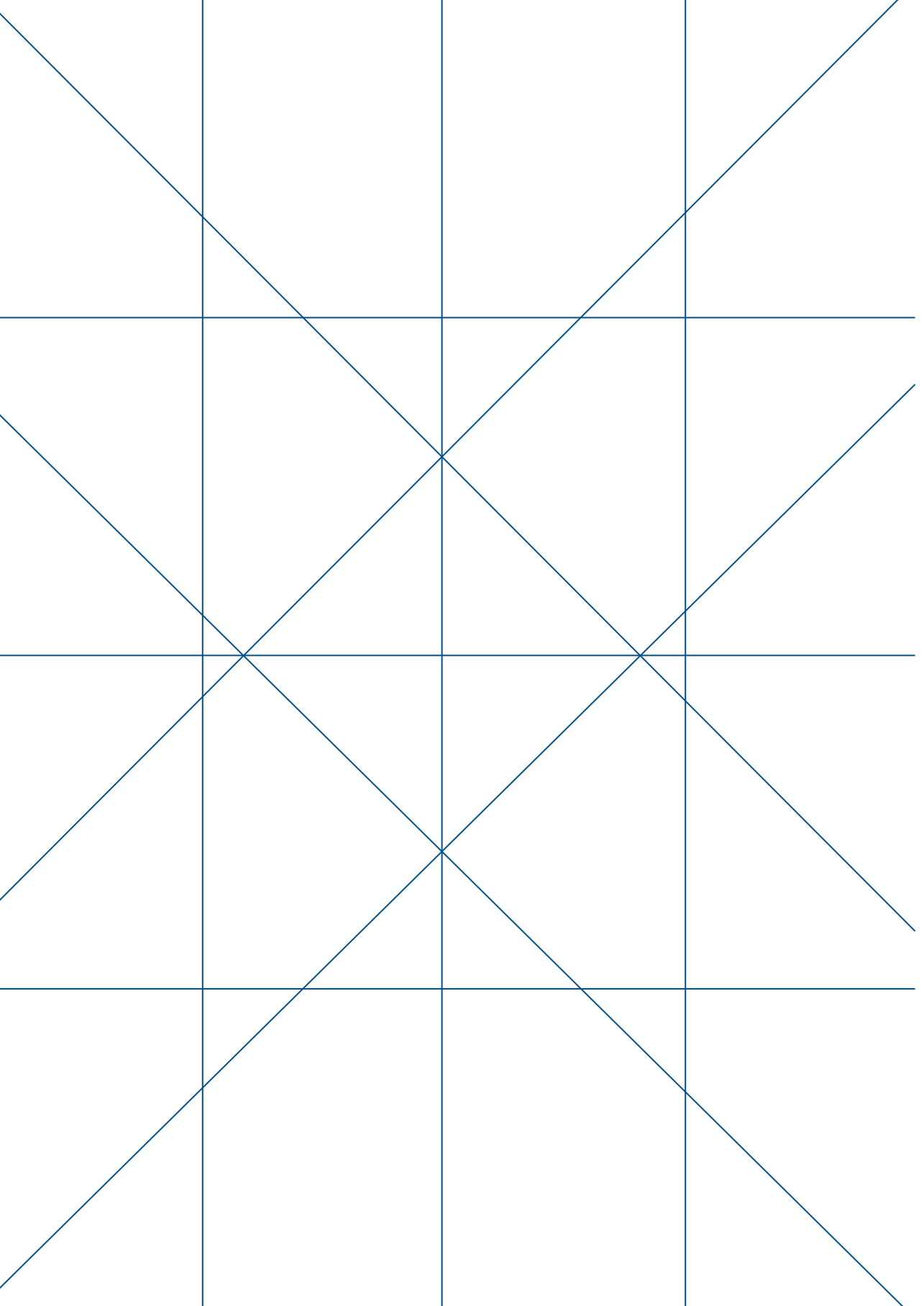
Hoofdstuk 7 behandelt een nationaal prospectief registercohort om de relatie tussen incarceratie van primaire buikenwandbreuken en littekenbreuken

betreffende defectgrootte evenals defectlocatie uit te zoeken. De prevalentie van een irreponibele incarceratie was 3,5 procent bij een totaal van 2352 patiënten met een primaire buikwandbreuken en 3,7 procent bij littekenbreuken bij een totaalaantal van 2120 patiënten. Voor beide typen breuken waren defecten van drie tot vier centimeter geassocieerd met incarceratie. Buikwandbreuken kleiner dan twee centimeter incarcereerden daarentegen zelden. Opmerkelijk was dat bij de patiënten met een primaire hernia van drie tot vier centimeter in tien procent van de gevallen incarceratie optrad. Bovendien was er alleen een associatie van incarceratie op niveau van de navel bij primaire buikwandbreuken en niet bij littekenbreuken. Leeftijd, *body mass index (BMI)* en factoren die zorgen voor een verhoogde intra-abdominale druk zijn voorbeelden van determinanten die in beide groepen met incarceratie geassocieerd waren. Interessant was dat ook het vrouwelijke geslacht bij patiënten met een littekenbreuk met incarceratie geassocieerd was. Een wetenschappelijk onderbouwde verklaring hiervoor werd niet gevonden.

Hoofdstuk 8 geeft een beschrijving weer van een reeks van 23 patiënten met extreem grote buikwandbreuken met domeinverlies, behandeld met botulinetoxine A, preoperatief progressief pneumoperitoneum (Goni Moreno techniek) en component separatie technieken. De combinatie van botulinetoxine A injecties en preoperatief progressief pneumoperitoneum kan een goede toevoeging zijn op de bestaande component separatie technieken en aldus helpen bij het spanningsloos sluiten van de fascie bij patiënten met een extreem grote buikwandbreuk. Het blijft een uitdaging om preoperatief te bepalen welke patiënt deze extra hulpmiddelen uiteindelijk nodig zal hebben. In deze studie is een gestandaardiseerd algoritme ontwikkeld voor patiënten met een extreem grote buikwandbreuk om zo te voorkomen dat de chirurg tijdens de operatie met onvoorziene moeilijkheden te maken krijgt. Het primair spanningsvrij sluiten van de voorste fascie was mogelijk in 82% van alle patiënten na een mediane *follow-up* van 19.5 maanden. Drie patiënten kregen een recidief en 16 patiënten hadden postoperatief wondproblemen, voornamelijk wondinfecties. Belangrijk om te beseffen is dat het in deze studie om patiënten gaat met veel co-morbiditeit en obesitas.

In **Hoofdstuk 9** werden de functionele uitkomsten bij symptomatische en asymptomatische patiënten na littekenbreukcorrectie in een prospectief

registercohort onderzocht. Ondanks het feit dat herstel van een littekenbreuk meestal resulteert in dat de patiënt van de klachten af is, kan een operatie ook leiden tot behoud van klachten of juist nieuwe klachten induceren. Preoperatief symptomatische patiënten (n = 1091) rapporteerden in 28% van de gevallen pijn of ongemak na herstel van de hernia, na een gemiddelde *follow-up* van 11,3 maanden. Preoperatief asymptomatische patiënten (n = 221) rapporteerden in 20% van alle gevallen pijn of ongemak na herstel van de hernia na een gemiddelde follow-up van 10,5 maanden. Dit risico van het induceren van pijn of ongemak bij preoperatief asymptomatische patiënten moet uitvoerig met de patiënt worden besproken wanneer wordt besloten om al dan niet te opereren. Daarbij moet ook aan symptomatische patiënten preoperatief duidelijk uitgelegd worden dat er een risico bestaat dat ondanks operatie pijn en ongemak kunnen blijven bestaan.



Chapter 13

List of publications

List of contributing authors

Dankwoord

PhD portfolio

Curriculum Vitae

List of publications

Anatomical study comparing medialization after Rives-Stoppa, anterior component separation, and posterior component separation.
Y. Yurtkap, D. Sneiders (shared first author), L.F. Kroese, J. Jeekel, F.E. Muysoms, G.J. Kleinrensink, J.F. Lange
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Book Chapter
The Prevention of Incisional Hernias.
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The Art of Hernia Surgery, Springer, 2018

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PhD portfolio

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Supervisor	Prof. dr. J. Jeekel

PhD Training	**Year**	**ECTS**
Courses		
Endnote Course	2018	0.5
Systematic Literature Retrieval Pubmed	2018	1
SPSS Course	2018	1
Basiscursus Regelgeving Klinisch Onderzoek (BROK)	2018	1.5
Scientific Integrity	2018	0.3
Laboratory Animal Science (Artikel 9)	2018	3
pen Clinica Course	2019	1
Biomedical English Writing Course	2019	2
Presentations at inter(national) conferences		
Deutsche Herniengesellschaft, Hamburg, Germany	2018	1
Stichting Experimenteel Onderzoek Heelkundige Specialismen, Rotterdam,	2018	1
The Netherlands European Society for Surgical Research,	2019	2
Geneva, Switzerland European Hernia Society, Barcelona, Spain	2020	1
Stichting Experimenteel Onderzoek Heelkundige Specialismen, Amsterdam,	2019	1
The Netherlands		
Attendance at (inter)national conferences and seminars		
Wetenschapsdag Heelkunde, Erasmus MC,	2018	1
Rotterdam, the Netherlands Wetenschapsdag Heelkunde, Erasmus MC,	2019	1
Rotterdam, the Netherlands Wetenschapsdag Heelkunde, Erasmus MC,	2020	1
Rotterdam, the Netherlands Mesh Congress, Paris, France	2019	1
Rotterdam Interactive Congress on Hernia,	2019	1
Rotterdam, the Netherlands Wondcongres, Rotterdam, the Netherlands	2019	1
Other		
Organizing: Rotterdam Interactive Congress on Hernia, Rotterdam, theNetherlands	2019	2
REPAIR Research Meetings, weekly	2017-2019	3
Teaching anatomy (Snijzaal)	2018-2019	2
Supervision master thesis	2018	1
Total		**30.3**

Curriculum Vitae

Yağmur Yurtkap was born in Dordrecht on June 25th 1988. She grew up in Dordrecht and went to Johan de Witt Gymnasium from 2000 to 2006. She commenced medical school at the Erasmus University in 2007. With a growing interest in science, she participated in fundamental research at the neuroscience department under supervision of prof. dr. S.A. Kushner. Following her clinical rotations, she obtained her medical degree in April 2014. After graduation, Yağmur started as a resident not in training (ANIOS) at the Department of Surgery at the Franciscus Gasthuis Hospital (Rotterdam) under the supervision of dr. T.M.A.L. Klem. Next, she started with clinical research at the Katholieke Universiteit Leuven in Belgium under the supervision of prof. dr. M. Miserez during one year. Afterwards, she worked for a few months as a resident at the Maasstad Hospital in Rotterdam (drs. R.A. Klaassen). Finally, at the end of 2017, she started as a PhD candidate with the REsearch Projects for Abdominal surgery Innovation Rotterdam (REPAIR) group under the supervision of prof. dr. J.F. Lange, prof. dr. G.J. Kleinrensink, dr. A.G. Menon and prof. dr. J. Jeekel, which has led to this thesis. Despite her interest in science and surgery, she remains fascinated by the inner workings of the human brain and will for that reason start working in the psychiatry department, starting April 2020.